

STAD29: Statistics for the Life and Social Sciences

Lecture notes

Section 1

Course Outline

Course and instructor

- Lecture: Wednesday 14:00-16:00 in HW 215. Optional computer lab Monday 16:00-17:00 in BV 498.
- Instructor: Ken Butler
- Office: IC 471.
- E-mail: butler@utsc.utoronto.ca
- Office hours: Monday 11:00-13:00. I am often around otherwise. See if I'm in. Or make an appointment. E-mail always good.
- Course website: [link](#).
- Using Quercus for assignments/grades only; using website for everything else.

Texts

- There is no official text for this course.
- You may find “R for Data Science”, **link** helpful for R background.
- I will refer frequently to my book of Problems and Solutions in Applied Statistics (PASIAS), **link**.
- Both of these resources are and will remain free.

Programs, prerequisites and exclusions

- Prerequisites:
- For undergrads: STAC32. Not negotiable.
- For grad students, a first course in statistics, and some training in regression and ANOVA. The less you know, the more you'll have to catch up!
- This course is a required part of Applied Statistics minor.
- Exclusions: **this course is not for Math/Statistics/CS majors/minors**. It is for students in other fields who wish to learn some more advanced statistical methods. The exclusions in the Calendar reflect this.
- If you are in one of those programs, you won't get program credit for this course, **or for any future STA courses you take**.

Computing

- Computing: big part of the course, **not** optional. You will need to demonstrate that you can use R to analyze data, and can critically interpret the output.
- For grad students who have not come through STAC32, I am happy to offer extra help to get you up to speed.

Assessment 1/2

- Grading: (2 hour) midterm, (3 hour) final exam. Assignments most weeks, due Tuesday at 11:59pm. Graduate students (STA 1007) also required to complete a project using one or more of the techniques learned in class, on a dataset from their field of study. Projects due on the last day of classes.
- Assessment:

	STAD29	STA 1007
Assignments	20%	20%
Midterm exam	30%	20%
Project	-	20%
Final exam	50%	40%

Assessment 2/2

- Assessments missed *with documentation* will cause a re-weighting of other assessments of same type. No make-ups.
- You **must pass the final exam** to guarantee passing the course. If you fail the final exam but would otherwise have passed the course, you receive a grade of 45.

Plagiarism

- **This link** defines academic offences at this university. Read it. You are bound by it.
- Plagiarism defined (at the end) as
The wrongful appropriation and purloining, and publication as one's own, of the ideas, or the expression of the ideas ... of another.
- The code and explanations that you write and hand in must be *yours and yours alone*.
- When you hand in work, it is implied that it is *your* work. Handing in work, with your name on it, that was actually done by someone else is an *academic offence*.
- If I am suspicious that anyone's work is plagiarized, I will take action.

Getting help

- The English Language Development Centre supports all students in developing better Academic English and critical thinking skills needed in academic communication. Make use of the personalized support in academic writing skills development. Details and sign-up information: [link](#).
- Students with diverse learning styles and needs are welcome in this course. In particular, if you have a disability/health consideration that may require accommodations, please feel free to approach the AccessAbility Services Office as soon as possible. I will work with you and AccessAbility Services to ensure you can achieve your learning goals in this course. Enquiries are confidential. The UTSC AccessAbility Services staff are available by appointment to assess specific needs, provide referrals and arrange appropriate accommodations: (416) 287-7560 or by e-mail: ability@utsc.utoronto.ca.

Course material

- Regression-like things
 - review of (multiple) regression
 - logistic regression (including multi-category responses)
 - survival analysis
- ANOVA-like things
 - more ANOVA
 - multivariate ANOVA
 - repeated measures
- Multivariate methods
 - discriminant analysis
 - cluster analysis
 - multidimensional scaling
 - principal components
 - factor analysis
- Miscellanea
 - time series
 - multiway frequency tables

Section 2

Review of (multiple) regression

Regression

- Use regression when one variable is an outcome (*response*, y).
- See if/how response depends on other variable(s), *explanatory*, x_1, x_2, \dots
- Can have *one or more than one* explanatory variable, but always one response.
- Assumes a *straight-line* relationship between response and explanatory.
- Ask:
 - *is there* a relationship between y and x 's, and if so, which ones?
 - what does the relationship look like?

Packages

```
library(MASS) # for Box-Cox, later  
library(tidyverse)  
library(broom)
```

A regression with one x

13 children, measure average total sleep time (ATST, mins) and age (years) for each. See if ATST depends on age. Data in `sleep.txt`, ATST then age. Read in data:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/sleep.txt"
sleep <- read_delim(my_url, " ")
```

```
## Parsed with column specification:
## cols(
##   atst = col_double(),
##   age = col_double()
## )
```

Check data

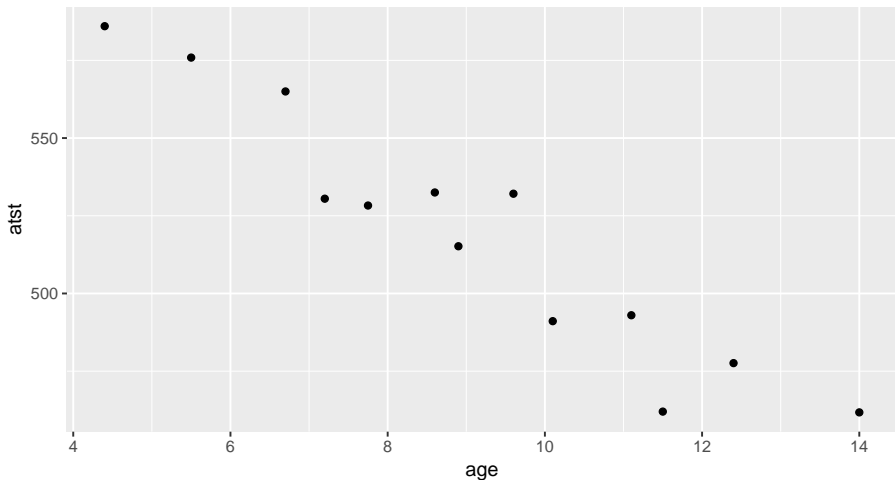
```
summary(sleep)
```

```
##           atst           age
##  Min.      :461.8   Min.      : 4.400
##  1st Qu.:491.1   1st Qu.: 7.200
##  Median :528.3   Median : 8.900
##  Mean     :519.3   Mean     : 9.058
##  3rd Qu.:532.5   3rd Qu.:11.100
##  Max.     :586.0   Max.     :14.000
```

Make scatter plot of ATST (response) vs. age (explanatory) using code
overleaf:

The scatterplot

```
ggplot(sleep, aes(x = age, y = atst)) + geom_point()
```



Correlation

- Measures how well a straight line fits the data:

```
with(sleep, cor(atst, age))
```

```
## [1] -0.9515469
```

- 1 is perfect upward trend, -1 is perfect downward trend, 0 is no trend.
- This one close to perfect downward trend.
- Can do correlations of all pairs of variables:

```
cor(sleep)
```

```
##           atst           age
## atst  1.0000000 -0.9515469
## age   -0.9515469  1.0000000
```

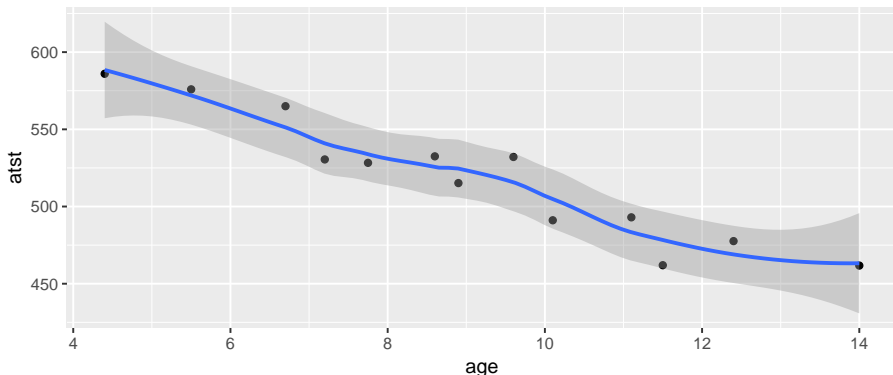
Lowess curve

- Sometimes nice to guide the eye: is the trend straight, or not?
- Idea: *lowess curve*. “Locally weighted least squares”, not affected by outliers, not constrained to be linear.
- Lowess is a *guide*: even if straight line appropriate, may wiggle/bend a little. Looking for *serious* problems with linearity.
- Add lowess curve to plot using `geom_smooth`:

Plot with lowess curve

```
ggplot(sleep, aes(x = age, y = atst)) + geom_point() +  
  geom_smooth()
```

`geom_smooth()` using method = 'loess' and formula 'y ~ x'



The regression

Scatterplot shows no obvious curve, and a pretty clear downward trend. So we can run the regression:

```
sleep.1 <- lm(atst ~ age, data = sleep)
```

The output

```
summary(sleep.1)
```

```
##
## Call:
## lm(formula = atst ~ age, data = sleep)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -23.011  -9.365   2.372   6.770  20.411
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  646.483     12.918   50.05 2.49e-14 ***
## age         -14.041       1.368  -10.26 5.70e-07 ***
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 13.15 on 11 degrees of freedom
## Multiple R-squared:  0.9054, Adjusted R-squared:  0.8968
## F-statistic: 105.3 on 1 and 11 DF,  p-value: 5.7e-07
```

Conclusions

- The relationship appears to be a straight line, with a downward trend.
- F -tests for model as a whole and t -test for slope (same) both confirm this (P-value $5.7 \times 10^{-7} = 0.00000057$).
- Slope is -14 , so a 1-year increase in age goes with a 14-minute decrease in ATST on average.
- R-squared is correlation squared (when one x anyway), between 0 and 1 (1 good, 0 bad).
- Here R-squared is 0.9054, pleasantly high.

Doing things with the regression output

- Output from regression (and eg. t -test) is all right to look at, but hard to extract and re-use information from.
- Package broom extracts info from model output in way that can be used in pipe (later):

```
tidy(sleep.1)
```

```
## # A tibble: 2 x 5
##   term          estimate std.error statistic  p.value
##   <chr>          <dbl>     <dbl>     <dbl>    <dbl>
## 1 (Intercept)    646.        12.9       50.0 2.49e-14
## 2 age          -14.0         1.37     -10.3 5.70e- 7
```


also one-line summary of model:

```
glance(sleep.1)
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>      <dbl> <dbl>      <dbl>    <dbl> <int>
## 1    0.905      0.897  13.2      105. 5.70e-7     2
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

Broom part 2

```
sleep.1 %>% augment(sleep) %>% slice(1:8)
```

```
## # A tibble: 8 x 9
##   atst    age .fitted .se.fit .resid   .hat .sigma .cooksd
##   <dbl> <dbl>   <dbl>   <dbl> <dbl>   <dbl> <dbl>   <dbl>
## 1  586    4.4   585.    7.34   1.30  0.312   13.8  0.00320
## 2  462.   14   450.    7.68  11.8  0.341   13.0  0.319
## 3  491.  10.1   505.    3.92 -13.6  0.0887  13.0  0.0568
## 4  565    6.7   552.    4.87  12.6  0.137   13.1  0.0844
## 5  462   11.5   485.    4.95 -23.0  0.141   11.3  0.294
## 6  532.    9.6   512.    3.72  20.4  0.0801  12.0  0.114
## 7  478.   12.4   472.    5.85   5.23  0.198   13.7  0.0243
## 8  515.    8.9   522.    3.65  -6.32  0.0772  13.6  0.0105
## # ... with 1 more variable: .std.resid <dbl>
```

Useful for plotting residuals against an x -variable.

CI for mean response and prediction intervals

Once useful regression exists, use it for prediction:

- To get a single number for prediction at a given x , substitute into regression equation, eg. age 10: predicted ATST is $646.48 - 14.04(10) = 506$ minutes.
- To express uncertainty of this prediction:
- *CI for mean response* expresses uncertainty about mean ATST for all children aged 10, based on data.
- *Prediction interval* expresses uncertainty about predicted ATST for a new child aged 10 whose ATST not known. More uncertain.
- Also do above for a child aged 5.

Intervals

- Make new data frame with these values for age

```
my.age <- c(10, 5)
ages.new <- tibble(age = my.age)
ages.new
```

```
## # A tibble: 2 x 1
##   age
##   <dbl>
## 1    10
## 2     5
```

- Feed into predict:

```
pc <- predict(sleep.1, ages.new, interval = "c")
pp <- predict(sleep.1, ages.new, interval = "p")
```

The intervals

Confidence intervals for mean response:

```
cbind(ages.new, pc)
```

##	age	fit	lwr	upr
## 1	10	506.0729	497.5574	514.5883
## 2	5	576.2781	561.6578	590.8984

Prediction intervals for new response:

```
cbind(ages.new, pp)
```

##	age	fit	lwr	upr
## 1	10	506.0729	475.8982	536.2475
## 2	5	576.2781	543.8474	608.7088

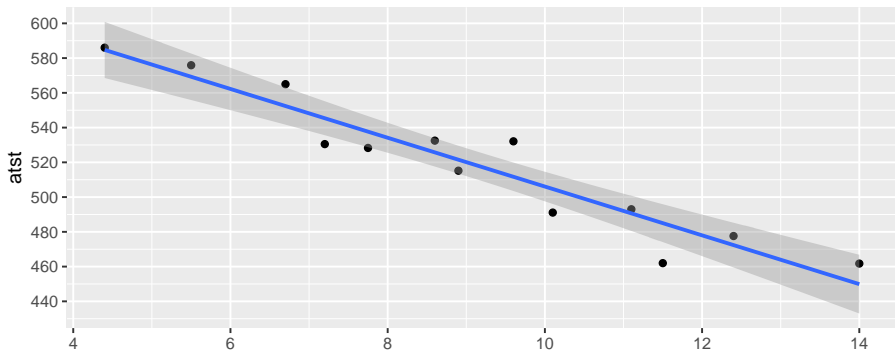
Comments

- Age 10 closer to centre of data, so intervals are both narrower than those for age 5.
- Prediction intervals bigger than CI for mean (additional uncertainty).
- Technical note: output from `predict` is R `matrix`, not data frame, so Tidyverse `bind_cols` does not work. Use base R `cbind`.

That grey envelope

Marks confidence interval for mean for all x :

```
ggplot(sleep, aes(x = age, y = atst)) + geom_point() +  
  geom_smooth(method = "lm") +  
  scale_y_continuous(breaks = seq(420, 600, 20))
```



Diagnostics

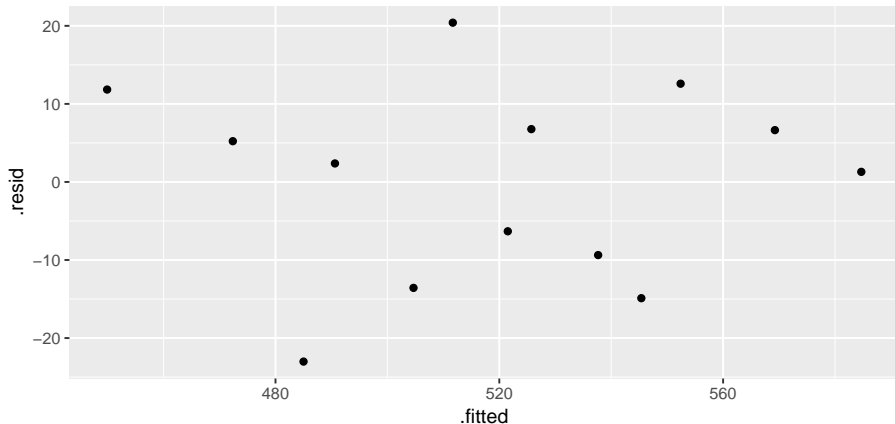
How to tell whether a straight-line regression is appropriate?

- Before: check scatterplot for straight trend.
- After: plot *residuals* (observed minus predicted response) against predicted values. Aim: a plot with no pattern.

Residual plot

Not much pattern here — regression appropriate.

```
ggplot(sleep.1, aes(x = .fitted, y = .resid)) + geom_point()
```



An inappropriate regression

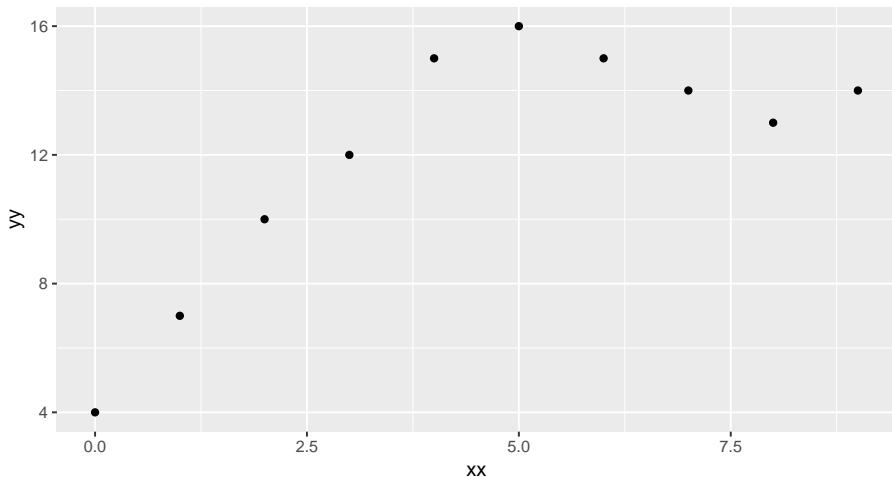
Different data:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/curvy.txt"  
curvy <- read_delim(my_url, " ")
```

```
## Parsed with column specification:  
## cols(  
##   xx = col_double(),  
##   yy = col_double()  
## )
```

Scatterplot

```
ggplot(curvy, aes(x = xx, y = yy)) + geom_point()
```



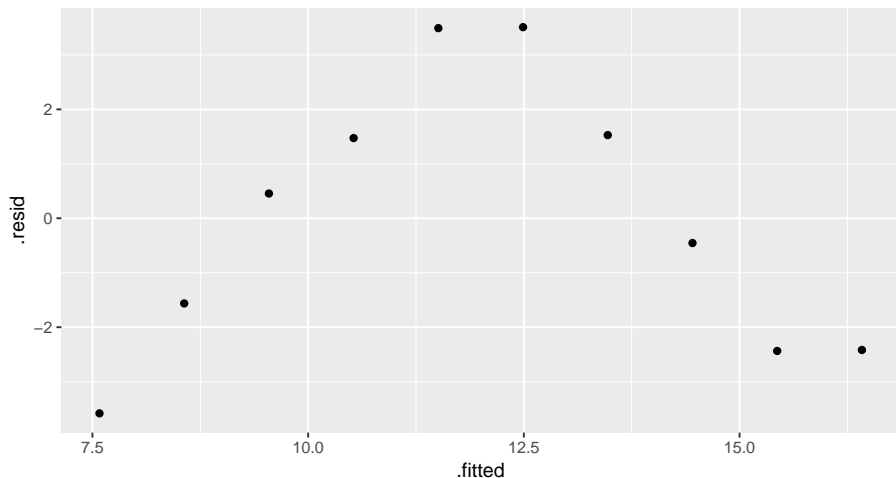
Regression line, anyway

```
curvy.1 <- lm(yy ~ xx, data = curvy)
summary(curvy.1)
```

```
##
## Call:
## lm(formula = yy ~ xx, data = curvy)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -3.582 -2.204  0.000  1.514  3.509
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   7.5818     1.5616   4.855  0.00126 **
## xx            0.9818     0.2925   3.356  0.00998 **
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 2.657 on 8 degrees of freedom
## Multiple R-squared:  0.5848, Adjusted R-squared:  0.5329
## F-statistic: 11.27 on 1 and 8 DF, p-value: 0.009984
```

Residual plot

```
ggplot(curvy.1, aes(x = .fitted, y = .resid)) + geom_point()
```



No good: fixing it up

- Residual plot has *curve*: middle residuals positive, high and low ones negative. Bad.
- Fitting a curve would be better. Try this:

```
curvy.2 <- lm(yy ~ xx + I(xx^2), data = curvy)
```

- Adding xx-squared term, to allow for curve.
- Another way to do same thing: specify how model *changes*:

```
curvy.2a <- update(curvy.1, . ~ . + I(xx^2))
```

Regression 2

```
tidy(curvy.2)
```

```
## # A tibble: 3 x 5
```

	term	estimate	std.error	statistic	p.value
	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
## 1	(Intercept)	3.9	0.773	5.04	0.00149
## 2	xx	3.74	0.400	9.36	0.0000331
## 3	I(xx^2)	-0.307	0.0428	-7.17	0.000182

```
glance(curvy.2) #
```

```
## # A tibble: 1 x 11
```

	r.squared	adj.r.squared	sigma	statistic	p.value	df
##	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<int>
## 1	0.950	0.936	0.983	66.8	2.75e-5	3

... with 5 more variables: logLik <dbl>, AIC <dbl>,
BIC <dbl>, deviance <dbl>, df.residual <int>

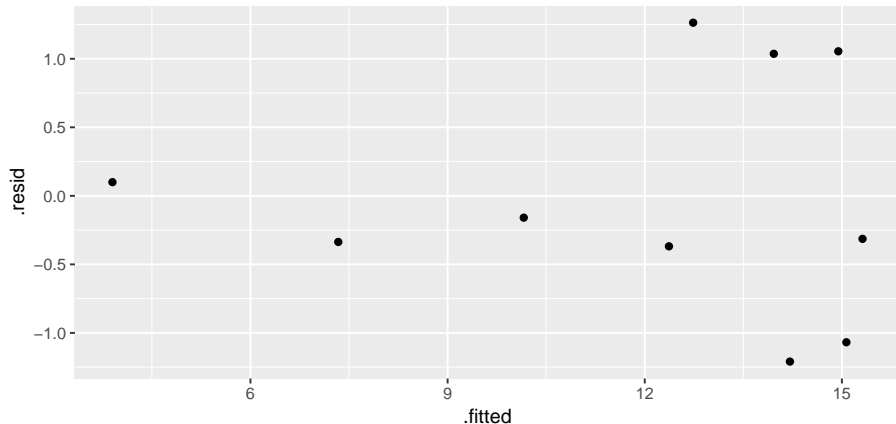
Comments

- xx -squared term definitely significant (P-value 0.000182), so need this curve to describe relationship.
- Adding squared term has made R-squared go up from 0.5848 to 0.9502: great improvement.
- This is a definite curve!

The residual plot now

No problems any more:

```
ggplot(curvy.2, aes(x = .fitted, y = .resid)) + geom_point()
```



Another way to handle curves

- Above, saw that changing x (adding x^2) was a way of handling curved relationships.
- Another way: change y (transformation).
- Can guess how to change y , or might be theory:
- example: relationship $y = ae^{bx}$ (exponential growth):
- take logs to get $\ln y = \ln a + bx$.
- Taking logs has made relationship linear ($\ln y$ as response).
- Or, *estimate* transformation, using Box-Cox method.

Box-Cox

- Install package MASS via `install.packages("MASS")` (only need to do *once*)
- Every R session you want to use something in MASS, type `library(MASS)`

Some made-up data

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/madeup.csv"
madeup <- read_csv(my_url)
madeup
```

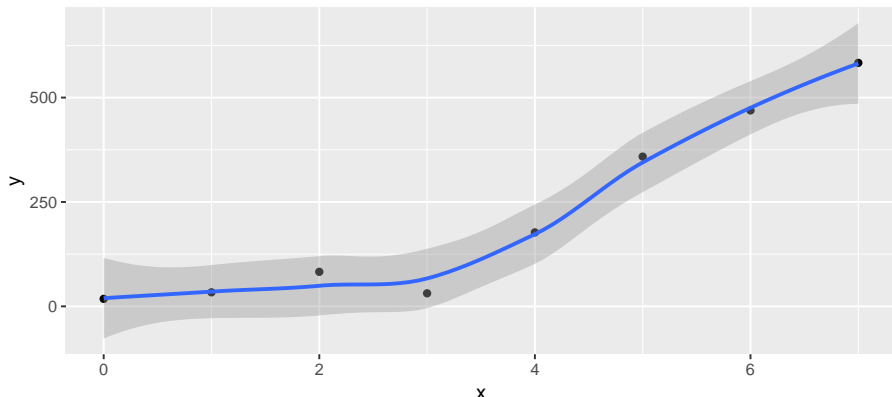
```
## # A tibble: 8 x 3
##   row      x      y
##   <dbl> <dbl> <dbl>
## 1     1     0  17.9
## 2     2     1  33.6
## 3     3     2  82.7
## 4     4     3  31.2
## 5     5     4 177.
## 6     6     5 359.
## 7     7     6 469.
## 8     8     7 583.
```

Seems to be faster-than-linear growth, maybe exponential growth.

Scatterplot: faster than linear growth

```
ggplot(madeup, aes(x = x, y = y)) + geom_point() +  
  geom_smooth()
```

```
## `geom_smooth()` using method = 'loess' and formula 'y ~ x'
```

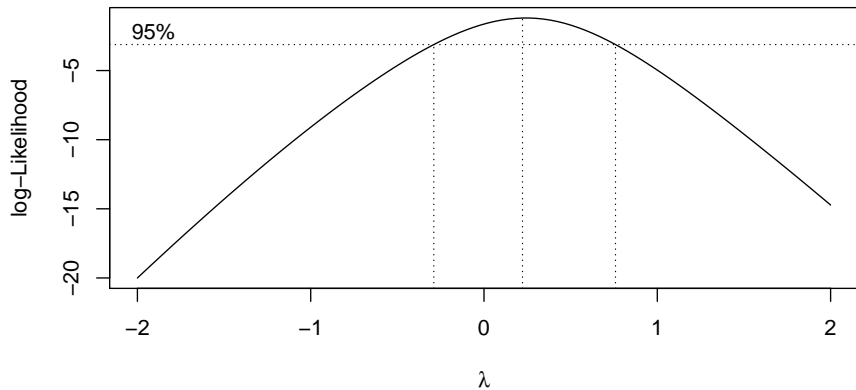


Running Box-Cox

- `library(MASS)` first.
- Feed `boxcox` a model formula with a squiggle in it, such as you would use for `lm`.
- Output: a graph (next page):

```
boxcox(y ~ x, data = madeup)
```

The Box-Cox output



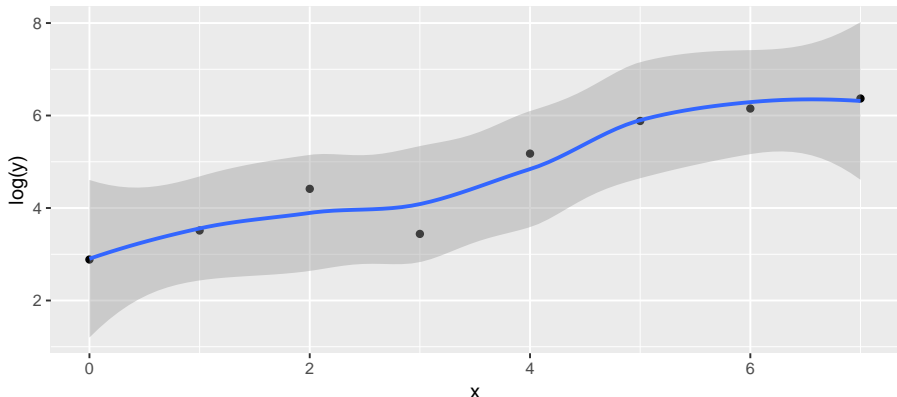
Comments

- λ (lambda) is the power by which you should transform y to get the relationship straight (straighter). Power 0 is “take logs”
- Middle dotted line marks best single value of λ (here about 0.1).
- Outer dotted lines mark 95% CI for λ , here -0.3 to 0.7 , approx. (Rather uncertain about best transformation.)
- Any power transformation within the CI supported by data. In this case, log ($\lambda = 0$) and square root ($\lambda = 0.5$) good, but no transformation ($\lambda = 1$) not.
- Pick a “round-number” value of λ like 2, 1, 0.5, 0, -0.5 , -1 . Here 0 and 0.5 good values to pick.

Did transformation straighten things?

- Plot transformed y against x . Here, log:

```
ggplot(madeup, aes(x = x, y = log(y))) + geom_point() +  
  geom_smooth()
```



Regression with transformed y

```
madeup.1 <- lm(log(y) ~ x, data = madeup)
glance(madeup.1)
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>      <dbl> <dbl>      <dbl>   <dbl> <int>
## 1     0.883        0.864 0.501        45.3 5.24e-4     2
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

```
tidy(madeup.1)
```

```
## # A tibble: 2 x 5
##   term          estimate std.error statistic  p.value
##   <chr>        <dbl>    <dbl>      <dbl>   <dbl>
## 1 (Intercept)    2.91    0.323      8.99 0.000106
## 2 x              0.520    0.0773     6.73 0.000524
```

R-squared now decently high.

Multiple regression

- What if more than one x ? Extra issues:
 - Now one intercept and a slope for each x : how to interpret?
 - Which x -variables actually help to predict y ?
 - Different interpretations of “global” F -test and individual t -tests.
 - R-squared no longer correlation squared, but still interpreted as “higher better”.
 - In `lm` line, add extra x s after `~`.
 - Interpretation not so easy (and other problems that can occur).

Multiple regression example

Study of women and visits to health professionals, and how the number of visits might be related to other variables:

timedrs: number of visits to health professionals (over course of study)

phyheal: number of physical health problems

menheal: number of mental health problems

stress: result of questionnaire about number and type of life changes

timedrs response, others explanatory.

The data

```
my_url <-  
  "http://www.uts.utoronto.ca/~butler/d29/regressx.txt"  
visits <- read_delim(my_url, " ")
```

```
## Parsed with column specification:  
## cols(  
##   subjno = col_double(),  
##   timedrs = col_double(),  
##   phyheal = col_double(),  
##   menheal = col_double(),  
##   stress = col_double()  
## )
```

Check data

```
visits
```

```
## # A tibble: 465 x 5
##   subjno timedrs phyheal menheal stress
##   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
## 1       1       1       5       8     265
## 2       2       3       4       6     415
## 3       3       0       3       4      92
## 4       4      13       2       2     241
## 5       5      15       3       6      86
## 6       6       3       5       5     247
## 7       7       2       5       6      13
## 8       8       0       4       5      12
## 9       9       7       5       4     269
## 10      10       4       3       9     391
## # ... with 455 more rows
```

Fit multiple regression

```
visits.1 <- lm(timedrs ~ phyheal + menheal + stress,
  data = visits)
glance(visits.1)
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>         <dbl> <dbl>      <dbl>    <dbl> <int>
## 1    0.219         0.214   9.71      43.0 1.56e-24     4
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

The slopes

Model as a whole strongly significant even though R-sq not very big (lots of data). At least one of the x 's predicts `timedrs`.

```
tidy(visits.1)
```

```
## # A tibble: 4 x 5
##   term          estimate std.error statistic  p.value
##   <chr>          <dbl>      <dbl>      <dbl>    <dbl>
## 1 (Intercept) -3.70         1.12      -3.30  1.06e- 3
## 2 phyheal      1.79         0.221      8.08  5.60e-15
## 3 menheal     -0.00967     0.129     -0.0749 9.40e- 1
## 4 stress       0.0136     0.00361     3.77  1.85e- 4
```

The physical health and stress variables initely help to predict the number of visits, but *with those in the model* we don't need `menheal`. However, look at prediction of `timedrs` from `menheal` by itself:

Just menheal

```
visits.2 <- lm(timedrs ~ menheal, data = visits)
glance(visits.2)
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>      <dbl> <dbl>      <dbl>  <dbl> <int>
## 1    0.0653      0.0633  10.6      32.4 2.28e-8     2
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

```
tidy(visits.2)
```

```
## # A tibble: 2 x 5
##   term          estimate std.error statistic    p.value
##   <chr>        <dbl>    <dbl>    <dbl>    <dbl>
## 1 (Intercept)    3.82     0.870     4.38 0.0000144
## 2 menheal        0.667    0.117     5.69 0.0000000228
```

menheal by itself

- menheal by itself *does* significantly help to predict timedrs.
- But the R-sq is much less (6.5% vs. 22%).
- So other two variables do a better job of prediction.
- With those variables in the regression (phyheal and stress), don't need menheal *as well*.

Investigating via correlation

Leave out first column (subjno):

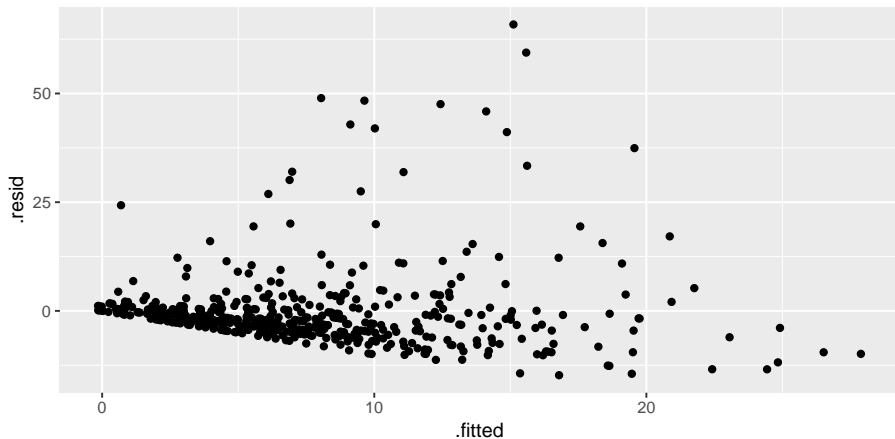
```
visits %>% select(-subjno) %>% cor()
```

```
##           timedrs   phyheal   menheal   stress
## timedrs  1.0000000  0.4395293  0.2555703  0.2865951
## phyheal  0.4395293  1.0000000  0.5049464  0.3055517
## menheal  0.2555703  0.5049464  1.0000000  0.3697911
## stress   0.2865951  0.3055517  0.3697911  1.0000000
```

- phyheal most strongly correlated with timedrs.
- Not much to choose between other two.
- But menheal has higher correlation with phyheal, so not as much to *add* to prediction as stress.
- Goes to show things more complicated in multiple regression.

Residual plot (from timedrs on all)

```
ggplot(visits.1, aes(x = .fitted, y = .resid)) + geom_point()
```

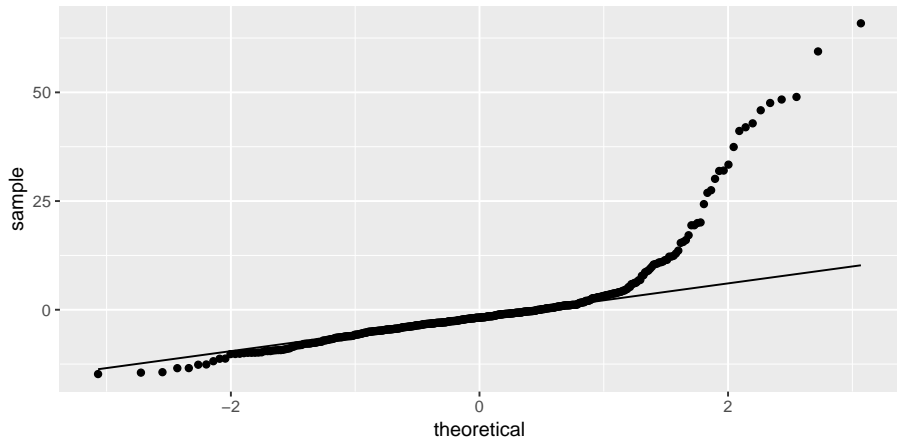


Comment

Apparently random. But...

Normal quantile plot of residuals

```
ggplot(visits.1, aes(sample = .resid)) + stat_qq() + stat_qq_line()
```

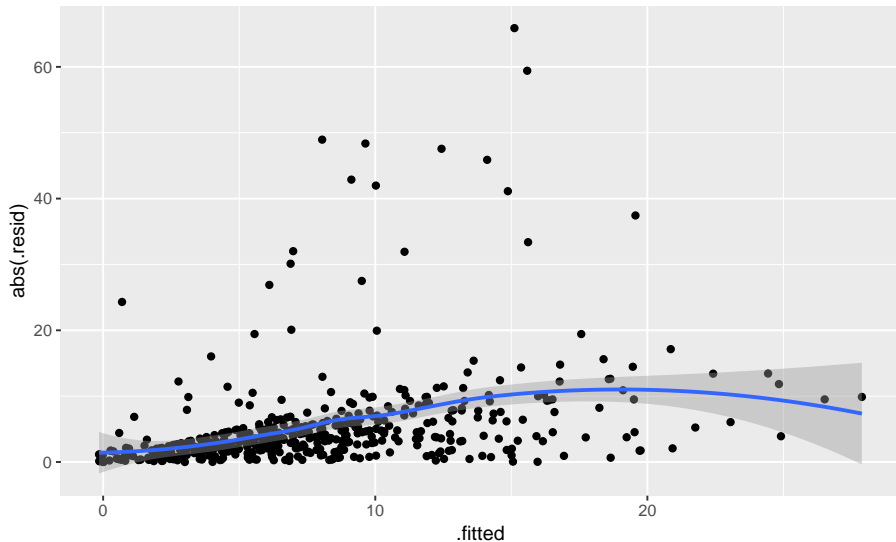


Absolute residuals

Is there trend in *size* of residuals (fan-out)? Plot *absolute value* of residual against fitted value (graph next page):

```
g <- ggplot(visits.1, aes(x = .fitted, y = abs(.resid))) +  
  geom_point() + geom_smooth()
```

The plot



Comments

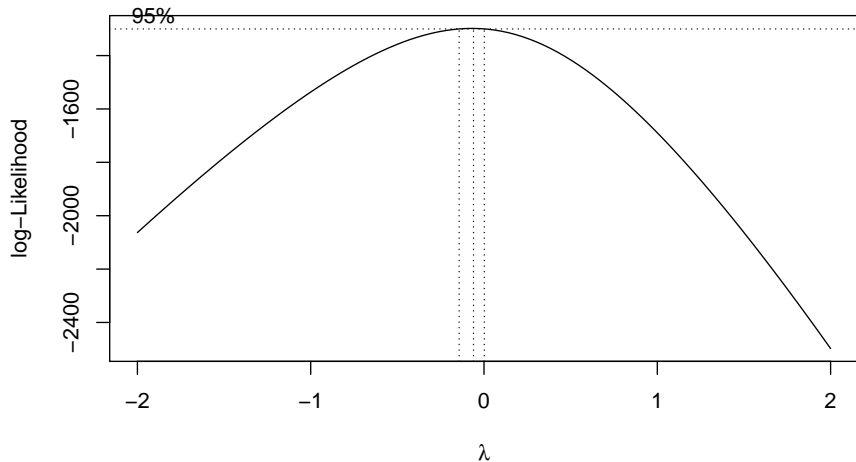
- On the normal quantile plot:
 - highest (most positive) residuals are way too high
 - distribution of residuals skewed to right (not normal at all)
- On plot of absolute residuals:
 - size of residuals getting bigger as fitted values increase
 - predictions getting more variable as fitted values increase
 - that is, predictions getting *less accurate* as fitted values increase, but predictions should be equally accurate all way along.
- Both indicate problems with regression, of kind that transformation of response often fixes: that is, predict *function* of response `timedrs` instead of `timedrs` itself.

Box-Cox transformations

- Taking log of `timedrs` and having it work: lucky guess. How to find good transformation?
- Box-Cox again.
- Extra problem: some of `timedrs` values are 0, but Box-Cox expects all $+$. Note response for `boxcox`:

```
boxcox(timedrs + 1 ~ phyheal + menheal + stress, data = visits)
```

Try 1



Comments on try 1

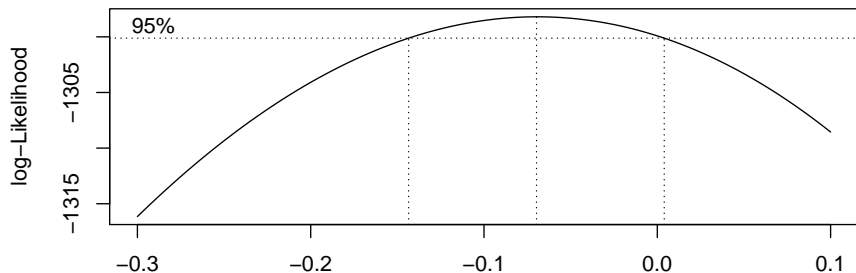
- Best: λ just less than zero.
- Hard to see scale.
- Focus on λ in $(-0.3, 0.1)$:

```
my.lambda <- seq(-0.3, 0.1, 0.01)
my.lambda
```

```
## [1] -0.30 -0.29 -0.28 -0.27 -0.26 -0.25 -0.24 -0.23 -0.22
## [10] -0.21 -0.20 -0.19 -0.18 -0.17 -0.16 -0.15 -0.14 -0.13
## [19] -0.12 -0.11 -0.10 -0.09 -0.08 -0.07 -0.06 -0.05 -0.04
## [28] -0.03 -0.02 -0.01  0.00  0.01  0.02  0.03  0.04  0.05
## [37]  0.06  0.07  0.08  0.09  0.10
```

Try 2

```
boxcox(timedrs + 1 ~ phyheal + menheal + stress,  
       lambda = my.lambda,  
       data = visits  
)
```



Comments

- Best: λ just about -0.07 .
- CI for λ about $(-0.14, 0.01)$.
- Only nearby round number: $\lambda = 0$, log transformation.

Fixing the problems

- Try regression again, with transformed response instead of original one.
- Then check residual plot to see that it is OK now.

```
visits.3 <- lm(log(timedrs + 1) ~ phyheal + menheal + stress,  
  data = visits  
)
```

- `timedrs+1` because some `timedrs` values 0, can't take log of 0.
- Won't usually need to worry about this, but when response could be zero/negative, fix that before transformation.

Output

```
summary(visits.3)
```

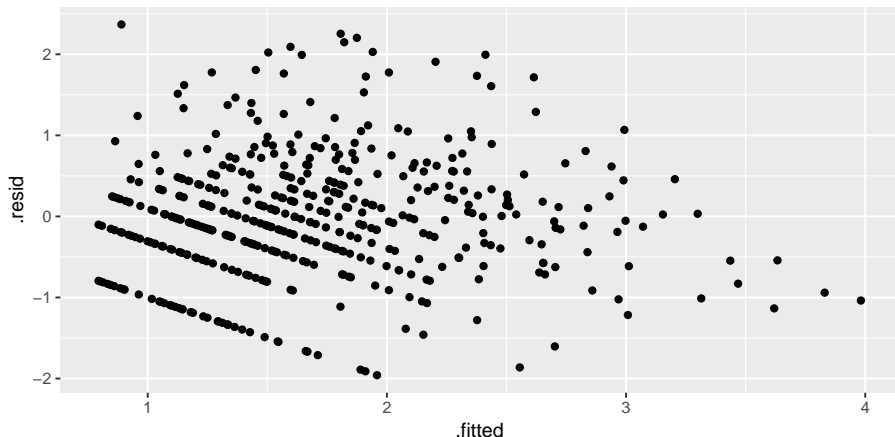
```
##
## Call:
## lm(formula = log(timedrs + 1) ~ phyheal + menheal + stress, data = visits)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.95865 -0.44076 -0.02331  0.42304  2.36797
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.3903862   0.0882908   4.422 1.22e-05 ***
## phyheal      0.2019361   0.0173624  11.631 < 2e-16 ***
## menheal      0.0071442   0.0101335   0.705  0.481
## stress       0.0013158   0.0002837   4.638 4.58e-06 ***
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.7625 on 461 degrees of freedom
## Multiple R-squared:  0.3682, Adjusted R-squared:  0.3641
## F-statistic: 89.56 on 3 and 461 DF,  p-value: < 2.2e-16
```


Comments

- Model as a whole strongly significant again
- R-sq higher than before (37% vs. 22%) suggesting things more linear now
- Same conclusion re `menheal`: can take out of regression.
- Should look at residual plots (next pages). Have we fixed problems?

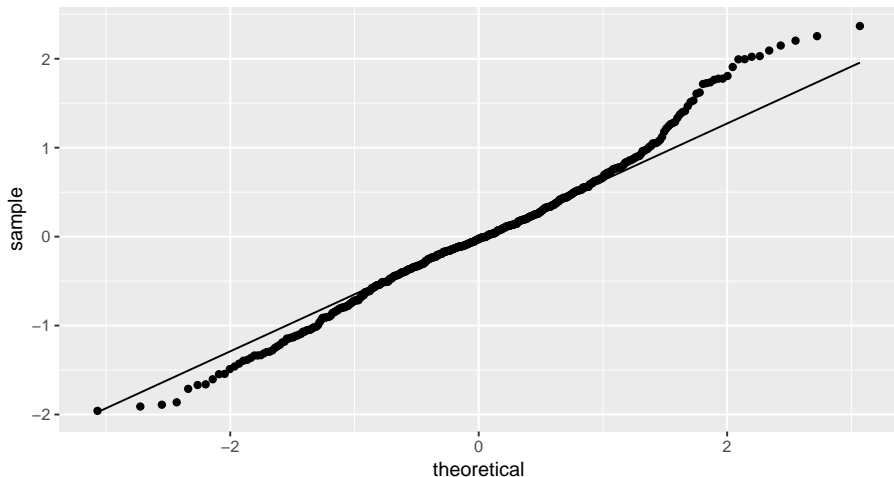
Residuals against fitted values

```
ggplot(visits.3, aes(x = .fitted, y = .resid)) +  
  geom_point()
```



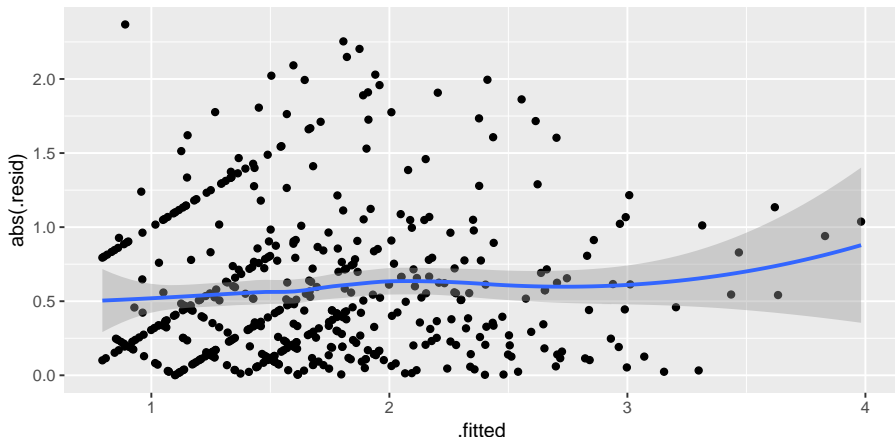
Normal quantile plot of residuals

```
ggplot(visits.3, aes(sample = .resid)) + stat_qq() + stat_qq_line()
```



Absolute residuals against fitted

```
ggplot(visits.3, aes(x = .fitted, y = abs(.resid))) +  
  geom_point() + geom_smooth()
```



Comments

- Residuals vs. fitted looks a lot more random.
- Normal quantile plot looks a lot more normal (though still a little right-skewness)
- Absolute residuals: not so much trend (though still some).
- Not perfect, but much improved.

Testing more than one x at once

- The t -tests test only whether one variable could be taken out of the regression you're looking at.
- To test significance of more than one variable at once, fit model with and without variables
 - then use anova to compare fit of models:

```
visits.5 <- lm(log(timedrs + 1) ~ phyheal + menheal + stress,  
              data = visits)  
visits.6 <- lm(log(timedrs + 1) ~ stress, data = visits)
```

Results of tests

```
anova(visits.6, visits.5)
```

```
## Analysis of Variance Table
##
## Model 1: log(timedrs + 1) ~ stress
## Model 2: log(timedrs + 1) ~ phyheal + menheal + stress
##   Res.Df    RSS Df Sum of Sq      F    Pr(>F)
## 1      463 371.47
## 2      461 268.01  2    103.46 88.984 < 2.2e-16 ***
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Models don't fit equally well, so bigger one fits better.
- Or “taking both variables out makes the fit worse, so don't do it”.
- Taking out those x 's is a mistake. Or putting them in is a good idea.

The punting data

Data set `punting.txt` contains 4 variables for 13 right-footed football kickers (punters): left leg and right leg strength (lbs), distance punted (ft), another variable called “fred”. Predict punting distance from other variables:

left	right	punt	fred
170	170	162.50	171
130	140	144.0	136
170	180	174.50	174
160	160	163.50	161
150	170	192.0	159
150	150	171.75	151
180	170	162.0	174
110	110	104.83	111
110	120	105.67	114
120	130	117.58	126
140	120	140.25	129
130	140	150.17	136
150	160	165.17	154

Reading in

- Separated by *multiple spaces* with *columns lined up*:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/punting.txt"
punting <- read_table(my_url)
```

```
## Parsed with column specification:
## cols(
##   left = col_double(),
##   right = col_double(),
##   punt = col_double(),
##   fred = col_double()
## )
```

The data

```
punting
```

```
## # A tibble: 13 x 4
##   left right  punt  fred
##   <dbl> <dbl> <dbl> <dbl>
## 1   170   170  162.   171
## 2   130   140  144    136
## 3   170   180  174.   174
## 4   160   160  164.   161
## 5   150   170  192    159
## 6   150   150  172.   151
## 7   180   170  162    174
## 8   110   110  105.   111
## 9   110   120  106.   114
## 10  120   130  118.   126
## 11  140   120  140.   129
## 12  130   140  150.   136
## 13  150   160  165.   154
```

Regression and output

```
punting.1 <- lm(punt ~ left + right + fred, data = punting)
glance(punting.1)
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>      <dbl> <dbl>    <dbl>  <dbl> <int>
## 1    0.778        0.704  14.7     10.5 0.00267     4
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

```
tidy(punting.1)
```

```
## # A tibble: 4 x 5
##   term          estimate std.error statistic p.value
##   <chr>          <dbl>    <dbl>    <dbl>  <dbl>
## 1 (Intercept)   -4.69      29.1     -0.161   0.876
## 2 left           0.268      2.11      0.127   0.902
## 3 right          1.05      2.15      0.490   0.636
## 4 fred          -0.267      4.23     -0.0632  0.951
```

Comments

- Overall regression strongly significant, R-sq high.
- None of the x 's significant! Why?
- t -tests only say that you could take any one of the x 's out without damaging the fit; doesn't matter which one.
- Explanation: look at *correlations*.

The correlations

```
cor(punting)
```

```
##           left      right      punt      fred
## left  1.0000000 0.8957224 0.8117368 0.9722632
## right 0.8957224 1.0000000 0.8805469 0.9728784
## punt  0.8117368 0.8805469 1.0000000 0.8679507
## fred  0.9722632 0.9728784 0.8679507 1.0000000
```

- All correlations are high: x 's with punt (good) and with each other (bad, at least confusing).
- What to do? Probably do just as well to pick one variable, say right since kickers are right-footed.

Just right

```
punting.2 <- lm(punt ~ right, data = punting)
anova(punting.2, punting.1)
```

```
## Analysis of Variance Table
##
## Model 1: punt ~ right
## Model 2: punt ~ left + right + fred
##   Res.Df    RSS Df Sum of Sq    F Pr(>F)
## 1      11 1962.5
## 2       9 1938.2  2    24.263 0.0563 0.9456
```

No significant loss by dropping other two variables.

Comparing R-squareds

```
summary(punting.1)$r.squared
```

```
## [1] 0.7781401
```

```
summary(punting.2)$r.squared
```

```
## [1] 0.7753629
```

Basically no difference. In regression (over), right significant:

Regression results

```
tidy(punting.2)
```

```
## # A tibble: 2 x 5
```

	term	estimate	std.error	statistic	p.value
	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
## 1	(Intercept)	-3.69	25.3	-0.146	0.886
## 2	right	1.04	0.169	6.16	0.0000709

But...

- Maybe we got the *form* of the relationship with `left` wrong.
- Check: plot *residuals* from previous regression (without `left`) against `left`.
- Residuals here are “punting distance adjusted for right leg strength”.
- If there is some kind of relationship with `left`, we should include in model.
- Plot of residuals against original variable: `augment` from `broom`.

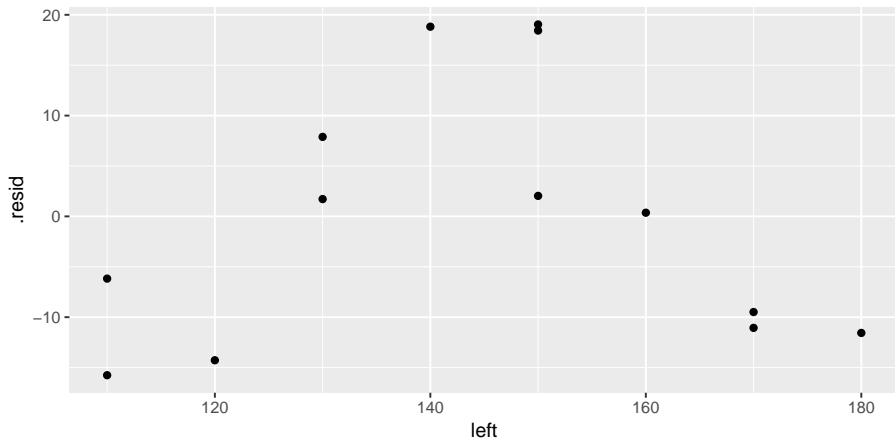
Augmenting punting.2

```
punting.2 %>% augment(punting) -> punting.2.aug
punting.2.aug %>% slice(1:8)
```

```
## # A tibble: 8 x 11
##   left right  punt  fred .fitted .se.fit .resid  .hat
##   <dbl> <dbl> <dbl> <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
## 1    170    170  162.   171    174.    5.29 -11.1   0.157
## 2    130    140  144.   136    142.    3.93  1.72  0.0864
## 3    170    180  174.   174    184.    6.60 -9.49  0.244
## 4    160    160  164.   161    163.    4.25  0.366 0.101
## 5    150    170  192.   159    174.    5.29 18.4   0.157
## 6    150    150  172.   151    153.    3.73 19.0   0.0778
## 7    180    170  162.   174    174.    5.29 -11.6   0.157
## 8    110    110  105.   111    111.    7.38 -6.17  0.305
## # ... with 3 more variables: .sigma <dbl>, .cooksd <dbl>,
## #   .std.resid <dbl>
```

Residuals against left

```
ggplot(punting.2.aug, aes(x = left, y = .resid)) +  
  geom_point()
```



Comments

- There is a *curved* relationship with left.
- We should add left-squared to the regression (and therefore put left back in when we do that):

```
punting.3 <- lm(punt ~ left + I(left^2) + right,  
  data = punting  
)
```

Regression with left-squared

```
summary(punting.3)
```

```
##
## Call:
## lm(formula = punt ~ left + I(left^2) + right, data = punting)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -11.3777  -5.3599   0.0459   4.5088  13.2669
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -4.623e+02  9.902e+01  -4.669  0.00117 **
## left         6.888e+00  1.462e+00   4.710  0.00110 **
## I(left^2)    -2.302e-02  4.927e-03  -4.672  0.00117 **
## right        7.396e-01  2.292e-01   3.227  0.01038 *
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 7.931 on 9 degrees of freedom
## Multiple R-squared:  0.9352, Adjusted R-squared:  0.9136
## F-statistic: 43.3 on 3 and 9 DF,  p-value: 1.13e-05
```

Comments

- This was definitely a good idea (R-squared has clearly increased).
- We would never have seen it without plotting residuals from `punting.2 (without left)` against `left`.
- Negative slope for `leftsq` means that increased left-leg strength only increases punting distance up to a point: beyond that, it decreases again.

Section 3

Logistic regression (ordinal/nominal response)

Logistic regression

- When response variable is measured/counted, regression can work well.
- But what if response is yes/no, lived/died, success/failure?
- Model *probability* of success.
- Probability must be between 0 and 1; need method that ensures this.
- *Logistic regression* does this. In R, is a *generalized linear model* with binomial “family”:

```
glm(y ~ x, family="binomial")
```

- Begin with simplest case.

Packages

```
library(MASS)  
library(tidyverse)  
library(broom)  
library(nnet)
```

The rats, part 1

- Rats given dose of some poison; either live or die:

dose status

0 lived

1 died

2 lived

3 lived

4 died

5 died

Read in:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/rat.txt"
rats <- read_delim(my_url, " ")
```

```
## Parsed with column specification:
## cols(
##   dose = col_double(),
##   status = col_character()
## )
```

```
glimpse(rats)
```

```
## Observations: 6
## Variables: 2
## $ dose      <dbl> 0, 1, 2, 3, 4, 5
## $ status    <chr> "lived", "died", "lived", "lived", "died",...
```

Basic logistic regression

- Make response into a factor first:

```
rats2 <- rats %>% mutate(status = factor(status))
```

- then fit model:

```
status.1 <- glm(status ~ dose, family = "binomial", data = rats2)
```

Output

```
summary(status.1)
```

```
##
## Call:
## glm(formula = status ~ dose, family = "binomial", data = rats2)
##
## Deviance Residuals:
##      1      2      3      4      5      6
## 0.5835 -1.6254  1.0381  1.3234 -0.7880 -0.5835
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)   1.6841     1.7979   0.937   0.349
## dose         -0.6736     0.6140  -1.097   0.273
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 8.3178  on 5  degrees of freedom
## Residual deviance: 6.7728  on 4  degrees of freedom
## AIC: 10.773
##
## Number of Fisher Scoring iterations: 4
```

Interpreting the output

- Like (multiple) regression, get tests of significance of individual x 's
- Here not significant (only 6 observations).
- “Slope” for dose is negative, meaning that as dose increases, probability of event modelled (survival) decreases.

Output part 2: predicted survival probs

```
p <- predict(status.1, type = "response")
cbind(rats, p)
```

##	dose	status	p
## 1	0	lived	0.8434490
## 2	1	died	0.7331122
## 3	2	lived	0.5834187
## 4	3	lived	0.4165813
## 5	4	died	0.2668878
## 6	5	died	0.1565510

The rats, more

- More realistic: more rats at each dose (say 10).
- Listing each rat on one line makes a big data file.
- Use format below: dose, number of survivals, number of deaths.

dose	lived	died
0	10	0
1	7	3
2	6	4
3	4	6
4	2	8
5	1	9

- 6 lines of data correspond to 60 actual rats.
- Saved in `rat2.txt`.

These data

```
my_url <- "http://www.uts.utoronto.ca/~butler/d29/rat2.txt"
rat2 <- read_delim(my_url, " ")
```

```
## Parsed with column specification:
## cols(
##   dose = col_double(),
##   lived = col_double(),
##   died = col_double()
## )
```

```
rat2
```

```
## # A tibble: 6 x 3
##   dose lived died
##   <dbl> <dbl> <dbl>
## 1     0    10     0
## 2     1     7     3
## 3     2     6     4
## 4     3     4     6
## 5     4     2     8
## 6     5     1     9
```

Create response matrix:

- Each row contains *multiple* observations.
- Create *two-column* response:
 - #survivals in first column,
 - #deaths in second.

```
response <- with(rat2, cbind(lived, died))
response
```

```
##      lived died
## [1,]    10    0
## [2,]     7    3
## [3,]     6    4
## [4,]     4    6
## [5,]     2    8
## [6,]     1    9
```

- Response is R matrix:

```
class(response)
```

```
## [1] "matrix"
```

Fit logistic regression

- using response you just made:

```
rat2.1 <- glm(response ~ dose,  
  family = "binomial",  
  data = rat2  
)
```

Output

```
summary(rat2.1)
```

```
##
## Call:
## glm(formula = response ~ dose, family = "binomial", data = rat2)
##
## Deviance Residuals:
##      1      2      3      4      5      6
##  1.3421 -0.7916 -0.1034  0.1034  0.0389  0.1529
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)   2.3619     0.6719   3.515 0.000439 ***
## dose         -0.9448     0.2351  -4.018 5.87e-05 ***
## ---
## Signif. codes:
##  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 27.530  on 5  degrees of freedom
## Residual deviance:  2.474  on 4  degrees of freedom
## AIC: 18.94
##
```

Predicted survival probs

```
p <- predict(rat2.1, type = "response")
cbind(rat2, p)
```

##	dose	lived	died	p
## 1	0	10	0	0.9138762
## 2	1	7	3	0.8048905
## 3	2	6	4	0.6159474
## 4	3	4	6	0.3840526
## 5	4	2	8	0.1951095
## 6	5	1	9	0.0861238

Comments

- Significant effect of dose.
- Effect of larger dose is to *decrease* survival probability (“slope” negative; also see in decreasing predictions.)

Multiple logistic regression

- With more than one x , works much like multiple regression.
- Example: study of patients with blood poisoning severe enough to warrant surgery. Relate survival to other potential risk factors.
- Variables, 1=present, 0=absent:
 - survival (death from sepsis=1), response
 - shock
 - malnutrition
 - alcoholism
 - age (as numerical variable)
 - bowel infarction
- See what relates to death.

Read in data

```
my_url <-  
  "http://www.utsc.utoronto.ca/~butler/d29/sepsis.txt"  
sepsis <- read_delim(my_url, " ")
```

```
## Parsed with column specification:  
## cols(  
##   death = col_double(),  
##   shock = col_double(),  
##   malnut = col_double(),  
##   alcohol = col_double(),  
##   age = col_double(),  
##   bowelinf = col_double()  
## )
```


The data

```
sepsis
```

```
## # A tibble: 106 x 6
```

```
##      death shock malnut alcohol   age bowelinf
##      <dbl> <dbl>   <dbl>   <dbl> <dbl>   <dbl>
```

```
## 1      0      0      0      0     56      0
```

```
## 2      0      0      0      0     80      0
```

```
## 3      0      0      0      0     61      0
```

```
## 4      0      0      0      0     26      0
```

```
## 5      0      0      0      0     53      0
```

```
## 6      1      0      1      0     87      0
```

```
## 7      0      0      0      0     21      0
```

```
## 8      1      0      0      1     69      0
```

```
## 9      0      0      0      0     57      0
```

```
## 10     0      0      1      0     76      0
```

```
## # ... with 96 more rows
```

Fit model

```
sepsis.1 <- glm(death ~ shock + malnut + alcohol + age +  
  bowelinf,  
  family = "binomial",  
  data = sepsis  
)
```

Output part 1

```
tidy(sepsis.1)
```

```
## # A tibble: 6 x 5
##   term          estimate std.error statistic  p.value
##   <chr>          <dbl>      <dbl>      <dbl>    <dbl>
## 1 (Intercept)  -9.75        2.54       -3.84 0.000124
## 2 shock         3.67        1.16        3.15 0.00161
## 3 malnut        1.22        0.728       1.67 0.0948
## 4 alcohol       3.35        0.982       3.42 0.000635
## 5 age           0.0922      0.0303       3.04 0.00237
## 6 bowelinf      2.80        1.16        2.40 0.0162
```

- All P-values fairly small
- but malnut not significant: remove.

Removing malnut

```
sepsis.2 <- update(sepsis.1, . ~ . - malnut)
tidy(sepsis.2)
```

```
## # A tibble: 5 x 5
```

##	term	estimate	std.error	statistic	p.value
##	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
## 1	(Intercept)	-8.89	2.32	-3.84	0.000124
## 2	shock	3.70	1.10	3.35	0.000797
## 3	alcohol	3.19	0.917	3.47	0.000514
## 4	age	0.0898	0.0292	3.07	0.00211
## 5	bowelinf	2.39	1.07	2.23	0.0260

- Everything significant now.

Comments

- Most of the original x 's helped predict death. Only `malnut` seemed not to add anything.
- Removed `malnut` and tried again.
- Everything remaining is significant (though `bowelinf` actually became *less* significant).
- All coefficients are *positive*, so having any of the risk factors (or being older) *increases* risk of death.

Predictions from model without “malnut”

- A few chosen at random:

```
sepsis.pred <- predict(sepsis.2, type = "response")
d <- data.frame(sepsis, sepsis.pred)
myrows <- c(4, 1, 2, 11, 32)
slice(d, myrows)
```

##	death	shock	malnut	alcohol	age	bowelinf	sepsis.pred
## 1	0	0	0	0	26	0	0.001415347
## 2	0	0	0	0	56	0	0.020552383
## 3	0	0	0	0	80	0	0.153416834
## 4	1	0	0	1	66	1	0.931290137
## 5	1	0	0	1	49	0	0.213000997

Comments

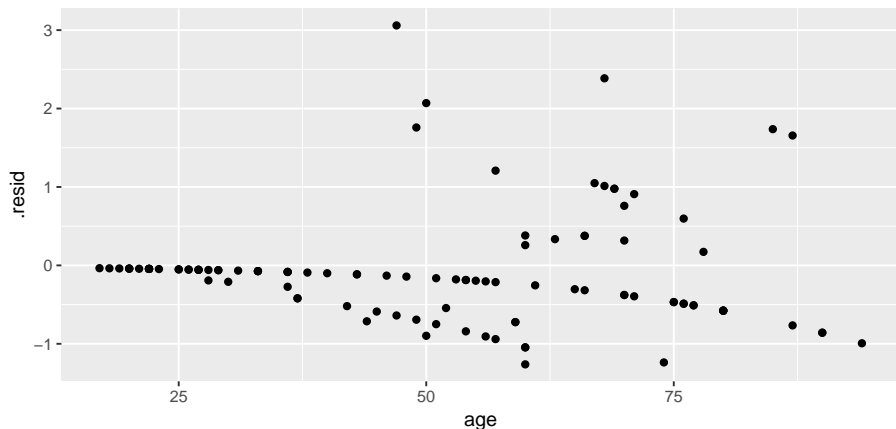
- Survival chances pretty good if no risk factors, though decreasing with age.
- Having more than one risk factor reduces survival chances dramatically.
- Usually good job of predicting survival; sometimes death predicted to survive.

Assessing proportionality of odds for age

- An assumption we made is that log-odds of survival depends linearly on age.
- Hard to get your head around, but basic idea is that survival chances go continuously up (or down) with age, instead of (for example) going up and then down.
- In this case, seems reasonable, but should check:

Residuals vs. age

```
ggplot(augment(sepsis.2), aes(x = age, y = .resid)) +  
  geom_point()
```



Comments

- No apparent problems overall.
- Confusing “line” across: no risk factors, survived.

Probability and odds

- For probability p , odds is $p/(1 - p)$:

Prob.	Odds	log-odds	in words
0.5	$0.5/0.5 = 1/1 = 1.00$	0.00	"even money"
0.1	$0.1/0.9 = 1/9 = 0.11$	-2.20	"9 to 1"
0.4	$0.4/0.6 = 1/1.5 = 0.67$	-0.41	"1.5 to 1"
0.8	$0.8/0.2 = 4/1 = 4.00$	1.39	"4 to 1 on"

- Gamblers use odds: if you win at 9 to 1 odds, get original stake back plus 9 times the stake.
- Probability has to be between 0 and 1
- Odds between 0 and infinity
- Log-odds* can be anything: any log-odds corresponds to valid probability.

Odds ratio

- Suppose 90 of 100 men drank wine last week, but only 20 of 100 women.
- Prob of man drinking wine $90/100 = 0.9$, woman $20/100 = 0.2$.
- Odds of man drinking wine $0.9/0.1 = 9$, woman $0.2/0.8 = 0.25$.
- Ratio of odds is $9/0.25 = 36$.
- Way of quantifying difference between men and women: “odds of drinking wine 36 times larger for males than females”.

Sepsis data again

- Recall prediction of probability of death from risk factors:

```
sepsis.2.tidy <- tidy(sepsis.2)
sepsis.2.tidy
```

```
## # A tibble: 5 x 5
```

##	term	estimate	std.error	statistic	p.value
##	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
## 1	(Intercept)	-8.89	2.32	-3.84	0.000124
## 2	shock	3.70	1.10	3.35	0.000797
## 3	alcohol	3.19	0.917	3.47	0.000514
## 4	age	0.0898	0.0292	3.07	0.00211
## 5	bowelinf	2.39	1.07	2.23	0.0260

- Slopes in column estimate.

Multiplying the odds

- Can interpret slopes by taking “exp” of them. We ignore intercept.

```
sepsis.2.tidy %>%
  mutate(exp_coef=exp(estimate)) %>%
  select(term, exp_coef)
```

```
## # A tibble: 5 x 2
##   term      exp_coef
##   <chr>      <dbl>
## 1 (Intercept) 0.000137
## 2 shock      40.5
## 3 alcohol    24.2
## 4 age        1.09
## 5 bowelinf   10.9
```

Interpretation

```
## # A tibble: 5 x 2
##   term          exp_coeff
##   <chr>          <dbl>
## 1 (Intercept)  0.000137
## 2 shock        40.5
## 3 alcohol      24.2
## 4 age           1.09
## 5 bowelinf     10.9
```

- These say “how much do you *multiply* odds of death by for increase of 1 in corresponding risk factor?” Or, what is odds ratio for that factor being 1 (present) vs. 0 (absent)?
- Eg. being alcoholic vs. not increases odds of death by 24 times
- One year older multiplies odds by about 1.1 times. Over 40 years, about $1.09^{40} = 31$ times.

Odds ratio and relative risk

- **Relative risk** is ratio of probabilities.
- Above: 90 of 100 men (0.9) drank wine, 20 of 100 women (0.2).
- Relative risk $0.9/0.2=4.5$. (odds ratio was 36).
- When probabilities small, relative risk and odds ratio similar.
- Eg. prob of man having disease 0.02, woman 0.01.
- Relative risk $0.02/0.01 = 2$.

Odds ratio vs. relative risk

- Odds for men and for women:

```
(od1 <- 0.02 / 0.98) # men
```

```
## [1] 0.02040816
```

```
(od2 <- 0.01 / 0.99) # women
```

```
## [1] 0.01010101
```

- Odds ratio

```
od1 / od2
```

```
## [1] 2.020408
```

- Very close to relative risk of 2.

More than 2 response categories

- With 2 response categories, model the probability of one, and prob of other is one minus that. So doesn't matter which category you model.
- With more than 2 categories, have to think more carefully about the categories: are they
 - *ordered*: you can put them in a natural order (like low, medium, high)
 - *nominal*: ordering the categories doesn't make sense (like red, green, blue).
- R handles both kinds of response; learn how.

Ordinal response: the miners

- Model probability of being in given category *or lower*.
- Example: coal-miners often suffer disease pneumoconiosis. Likelihood of disease believed to be greater among miners who have worked longer.
- Severity of disease measured on categorical scale: none, moderate, 3 severe.

Miners data

- Data are frequencies:

Exposure	None	Moderate	Severe
5.8	98	0	0
15.0	51	2	1
21.5	34	6	3
27.5	35	5	8
33.5	32	10	9
39.5	23	7	8
46.0	12	6	10
51.5	4	2	5

Reading the data

Data in aligned columns with more than one space between, so:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/miners-tab.txt"
freqs <- read_table(my_url)
```

```
## Parsed with column specification:
## cols(
##   Exposure = col_double(),
##   None = col_double(),
##   Moderate = col_double(),
##   Severe = col_double()
## )
```

The data

```
freqs
```

```
## # A tibble: 8 x 4
##   Exposure  None Moderate Severe
##   <dbl> <dbl>    <dbl> <dbl>
## 1     5.8    98         0      0
## 2     15    51         2      1
## 3    21.5   34         6      3
## 4    27.5   35         5      8
## 5    33.5   32        10      9
## 6    39.5   23         7      8
## 7     46    12         6     10
## 8    51.5    4         2      5
```

Tidying and row proportions

```
freqs %>%  
  gather(Severity, Freq, None:Severe) %>%  
  group_by(Exposure) %>%  
  mutate(proportion = Freq / sum(Freq)) -> miners
```

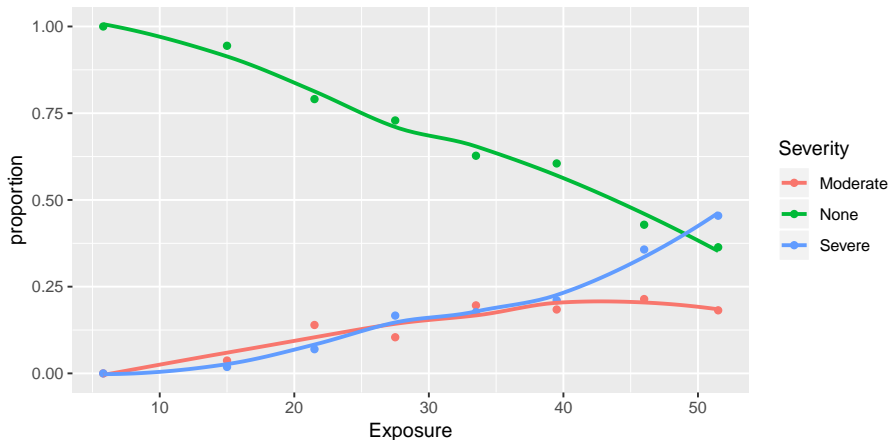
Result

```
miners
```

```
## # A tibble: 24 x 4
## # Groups:   Exposure [8]
##   Exposure Severity  Freq proportion
##   <dbl> <chr>      <dbl>      <dbl>
## 1     5.8 None         98         1
## 2     15  None         51      0.944
## 3    21.5 None         34      0.791
## 4    27.5 None         35      0.729
## 5    33.5 None         32      0.627
## 6    39.5 None         23      0.605
## 7     46  None         12      0.429
## 8    51.5 None          4      0.364
## 9     5.8 Moderate      0         0
## 10    15  Moderate      2      0.0370
## # ... with 14 more rows
```


Plot proportions against exposure

```
ggplot(miners, aes(x = Exposure, y = proportion,
                   colour = Severity)) +
  geom_point() + geom_smooth(se = F)
```



Reminder of data setup

```
miners
```

```
## # A tibble: 24 x 4
## # Groups:   Exposure [8]
##   Exposure Severity Freq proportion
##   <dbl> <chr>    <dbl>    <dbl>
## 1     5.8 None      98      1
## 2     15  None      51     0.944
## 3    21.5 None      34     0.791
## 4    27.5 None      35     0.729
## 5    33.5 None      32     0.627
## 6    39.5 None      23     0.605
## 7     46  None      12     0.429
## 8    51.5 None       4     0.364
## 9     5.8 Moderate    0     0
## 10    15  Moderate    2    0.0370
## # ... with 14 more rows
```

Creating an ordered factor

- Problem: on plot, Severity categories in *wrong order*.
- *In the data frame*, categories in *correct* order.
- Package `forcats` (in `tidyverse`) has functions for creating factors to specifications.
- `fct_inorder` takes levels *in order they appear in data*:

```
miners %>%
  mutate(sev_ord = fct_inorder(Severity)) -> miners
```

- To check:

```
levels(miners$sev_ord)
```

```
## [1] "None"      "Moderate" "Severe"
```

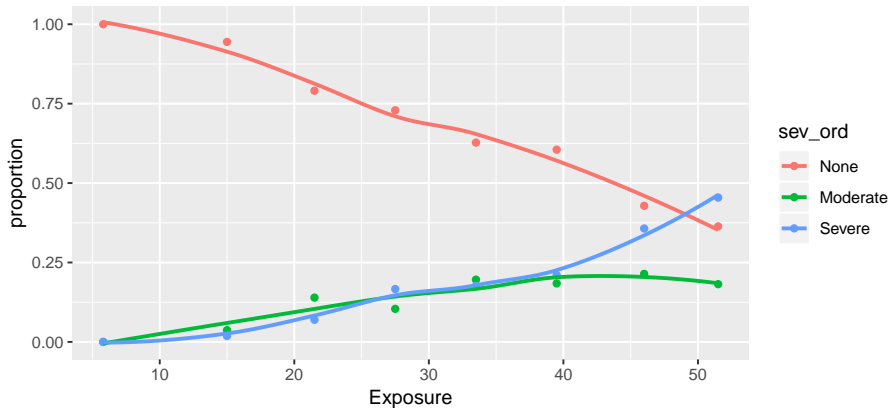
New data frame

```
miners
```

```
## # A tibble: 24 x 5
## # Groups:   Exposure [8]
##   Exposure Severity   Freq proportion sev_ord
##   <dbl> <chr>     <dbl>     <dbl> <fct>
## 1     5.8 None        98         1     None
## 2     15  None        51       0.944  None
## 3    21.5 None        34       0.791  None
## 4    27.5 None        35       0.729  None
## 5    33.5 None        32       0.627  None
## 6    39.5 None        23       0.605  None
## 7     46  None        12       0.429  None
## 8    51.5 None         4       0.364  None
## 9     5.8 Moderate     0         0     Moderate
## 10    15  Moderate     2      0.0370  Moderate
## # ... with 14 more rows
```

Improved plot

```
ggplot(miners, aes(x = Exposure, y = proportion,
                   colour = sev_ord)) +
  geom_point() + geom_smooth(se = F)
```



Fitting ordered logistic model

Use function `polr` from package `MASS`. Like `glm`.

```
sev.1 <- polr(sev_ord ~ Exposure,  
  weights = Freq,  
  data = miners  
)
```

Output: not very illuminating

```
summary(sev.1)
```

```
##
## Re-fitting to get Hessian

## Call:
## polr(formula = sev_ord ~ Exposure, data = miners, weights = Freq)
##
## Coefficients:
##              Value Std. Error t value
## Exposure 0.0959    0.01194    8.034
##
## Intercepts:
##              Value  Std. Error t value
## None|Moderate   3.9558   0.4097    9.6558
## Moderate|Severe 4.8690   0.4411   11.0383
##
## Residual Deviance: 416.9188
## AIC: 422.9188
```

Does exposure have an effect?

Fit model without Exposure, and compare using anova. Note 1 for model with just intercept:

```
sev.0 <- polr(sev_ord ~ 1, weights = Freq, data = miners)
anova(sev.0, sev.1)
```

```
## Likelihood ratio tests of ordinal regression models
##
## Response: sev_ord
##      Model Resid. df Resid. Dev   Test
## 1          1      369    505.1621
## 2 Exposure      368    416.9188 1 vs 2
##      Df LR stat. Pr(Chi)
## 1
## 2      1 88.24324      0
```

Exposure definitely has effect on severity of disease.

Another way

- What (if anything) can we drop from model with exposure?

```
drop1(sev.1, test = "Chisq")
```

```
## Single term deletions
##
## Model:
## sev_ord ~ Exposure
##           Df      AIC      LRT  Pr(>Chi)
## <none>      422.92
## Exposure   1 509.16 88.243 < 2.2e-16 ***
## ---
## Signif. codes:
##   0 '***' 0.001 '**' 0.01 '*' 0.05
##   '.' 0.1 ' ' 1
```

- Nothing. Exposure definitely has effect.

Predicted probabilities

Make new data frame out of all the exposure values (from original data frame), and predict from that:

```
sev.new <- tibble(Exposure = freqs$Exposure)
pr <- predict(sev.1, sev.new, type = "p")
miners.pred <- cbind(sev.new, pr)
miners.pred
```

##	Exposure	None	Moderate	Severe
## 1	5.8	0.9676920	0.01908912	0.01321885
## 2	15.0	0.9253445	0.04329931	0.03135614
## 3	21.5	0.8692003	0.07385858	0.05694115
## 4	27.5	0.7889290	0.11413004	0.09694093
## 5	33.5	0.6776641	0.16207145	0.16026444
## 6	39.5	0.5418105	0.20484198	0.25334756
## 7	46.0	0.3879962	0.22441555	0.38758828
## 8	51.5	0.2722543	0.21025011	0.51749563

Comments

- Model appears to match data: as exposure goes up, prob of None goes down, Severe goes up (sharply for high exposure).
- Like original data frame, this one nice to look at but *not tidy*. We want to make graph, so tidy it.
- Also want the severity values in right order.
- Usual gather, plus a bit:

```
miners.pred %>%  
  gather(Severity, probability, -Exposure) %>%  
  mutate(sev_ord = fct_inorder(Severity)) -> preds
```

Some of the gathered predictions

```
preds %>% slice(1:15)
```

##	Exposure	Severity	probability	sev_ord
## 1	5.8	None	0.96769203	None
## 2	15.0	None	0.92534455	None
## 3	21.5	None	0.86920028	None
## 4	27.5	None	0.78892903	None
## 5	33.5	None	0.67766411	None
## 6	39.5	None	0.54181046	None
## 7	46.0	None	0.38799618	None
## 8	51.5	None	0.27225426	None
## 9	5.8	Moderate	0.01908912	Moderate
## 10	15.0	Moderate	0.04329931	Moderate
## 11	21.5	Moderate	0.07385858	Moderate
## 12	27.5	Moderate	0.11413004	Moderate
## 13	33.5	Moderate	0.16207145	Moderate
## 14	39.5	Moderate	0.20484198	Moderate
## 15	46.0	Moderate	0.22441555	Moderate

Plotting predicted and observed proportions

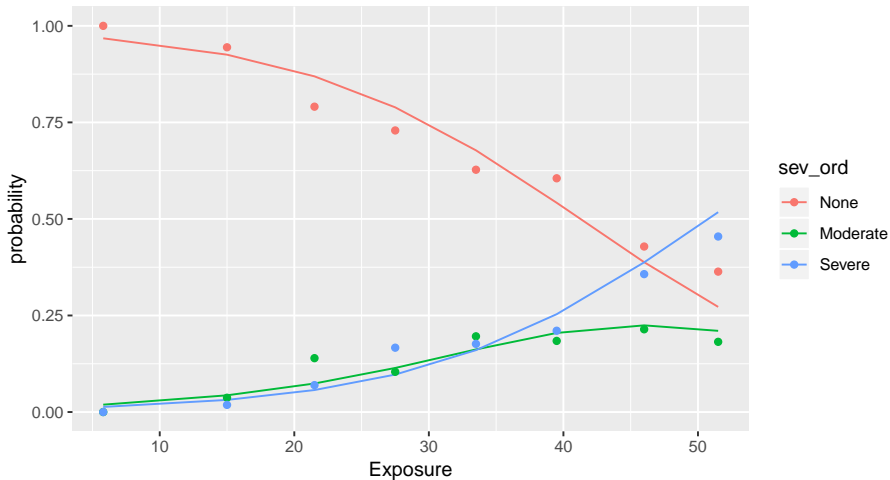
- Plot:
 - predicted probabilities, lines (shown) joining points (not shown)
 - data, just the points.
- Unfamiliar process: data from two *different* data frames:

```
g <- ggplot(preds, aes(
  x = Exposure, y = probability,
  colour = sev_ord
)) + geom_line() +
  geom_point(data = miners, aes(y = proportion))
```

- Idea: final `geom_point` uses data in `miners` rather than `preds`, y -variable for plot is `proportion` from that data frame, but x -coordinate is `Exposure`, as it was before, and `colour` is `Severity` as before. The final `geom_point` “inherits” from the first `aes` as needed.

The plot: data match model

g



Unordered responses

- With unordered (nominal) responses, can use *generalized logit*.
- Example: 735 people, record age and sex (male 0, female 1), which of 3 brands of some product preferred.
- Data in `mlogit.csv` separated by commas (so `read_csv` will work):

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/mlogit.csv"
brandpref <- read_csv(my_url)
```

```
## Parsed with column specification:
## cols(
##   brand = col_double(),
##   sex = col_double(),
##   age = col_double()
## )
```

The data

```
brandpref
```

```
## # A tibble: 735 x 3
##   brand    sex    age
##   <dbl> <dbl> <dbl>
## 1      1      0    24
## 2      1      0    26
## 3      1      0    26
## 4      1      1    27
## 5      1      1    27
## 6      3      1    27
## 7      1      0    27
## 8      1      0    27
## 9      1      1    27
## 10     1      0    27
## # ... with 725 more rows
```


Bashing into shape, and fitting model

- sex and brand not meaningful as numbers, so turn into factors:

```
brandpref <- brandpref %>%
  mutate(sex = factor(sex)) %>%
  mutate(brand = factor(brand))
```

- We use multinom from package nnet. Works like polr.

```
brands.1 <- multinom(brand ~ age + sex, data = brandpref)
```

```
## # weights: 12 (6 variable)
## initial value 807.480032
## iter 10 value 702.976983
## final value 702.970704
## converged
```

Can we drop anything?

- Unfortunately drop1 seems not to work:

```
drop1(brands.1, test = "Chisq", trace = 0)
```

```
## trying - age
```

```
## Error in if (trace) {: argument is not interpretable as logical
```

- so fall back on fitting model without what you want to test, and comparing using anova.

Do age/sex help predict brand? 1/2

Fit models without each of age and sex:

```
brands.2 <- multinom(brand ~ age, data = brandpref)
```

```
## # weights:  9 (4 variable)
## initial  value 807.480032
## iter   10 value 706.796323
## iter   10 value 706.796322
## final   value 706.796322
## converged
```

```
brands.3 <- multinom(brand ~ sex, data = brandpref)
```

```
## # weights:  9 (4 variable)
## initial  value 807.480032
## final   value 791.861266
## converged
```

Do age/sex help predict brand? 2/2

```
anova(brands.2, brands.1)
```

```
## Likelihood ratio tests of Multinomial Models
```

```
##
```

```
## Response: brand
```

##	Model	Resid. df	Resid. Dev	Test	Df	LR stat.	Pr(Chi)
## 1	age	1466	1413.593				
## 2	age + sex	1464	1405.941	1 vs 2	2	7.651236	0.02180495

```
anova(brands.3, brands.1)
```

```
## Likelihood ratio tests of Multinomial Models
```

```
##
```

```
## Response: brand
```

##	Model	Resid. df	Resid. Dev	Test	Df	LR stat.	Pr(Chi)
## 1	sex	1466	1583.723				
## 2	age + sex	1464	1405.941	1 vs 2	2	177.7811	0

Do age/sex help predict brand? 3/3

- age definitely significant (second anova)
- sex seems significant also (first anova)
- Keep both.

Another way to build model

- Start from model with everything and run step:

```
step(brands.1, trace = 0)
```

```
## trying - age
```

```
## trying - sex
```

```
## Call:
```

```
## multinom(formula = brand ~ age + sex, data = brandpref)
```

```
##
```

```
## Coefficients:
```

```
## (Intercept)      age      sex1
```

```
## 2    -11.77469 0.3682075 0.5238197
```

```
## 3    -22.72141 0.6859087 0.4659488
```

```
##
```

```
## Residual Deviance: 1405.941
```

```
## AIC: 1417.941
```

- Final model contains both age and sex so neither could be removed.

Predictions: all possible combinations

Create data frame with various age and sex:

```
ages <- c(24, 28, 32, 35, 38)
sexes <- factor(0:1)
new <- crossing(age = ages, sex = sexes)
new
```

```
## # A tibble: 10 x 2
##       age sex
##   <dbl> <fct>
## 1    24  0
## 2    24  1
## 3    28  0
## 4    28  1
## 5    32  0
## 6    32  1
## 7    35  0
## 8    35  1
## 9    38  0
## 10   38  1
```

Making predictions

```
p <- predict(brands.1, new, type = "probs")  
probs <- cbind(new, p)
```

or

```
p %>% as_tibble() %>%  
  bind_cols(new) -> probs
```


The predictions

```
probs
```

```
## # A tibble: 10 x 5
##       `1`      `2`      `3`    age sex
##   <dbl> <dbl> <dbl> <dbl> <fct>
## 1 0.948 0.0502 0.00181    24 0
## 2 0.915 0.0819 0.00279    24 1
## 3 0.793 0.183 0.0236     28 0
## 4 0.696 0.271 0.0329     28 1
## 5 0.405 0.408 0.187      32 0
## 6 0.291 0.495 0.214      32 1
## 7 0.131 0.397 0.472      35 0
## 8 0.0840 0.432 0.484      35 1
## 9 0.0260 0.239 0.735      38 0
## 10 0.0162 0.252 0.732      38 1
```

- Young males ($\text{sex}=0$) prefer brand 1, but older males prefer brand 3.
- Females similar, but like brand 1 less and brand 2 more.

Making a plot

- Plot fitted probability against age, distinguishing brand by colour and gender by plotting symbol.
- Also join points by lines, and distinguish lines by gender.
- I thought about facetting, but this seems to come out clearer.
- First need tidy data frame, by familiar process:

```
probs %>%  
  gather(brand, probability, -(age:sex)) -> probs.long
```

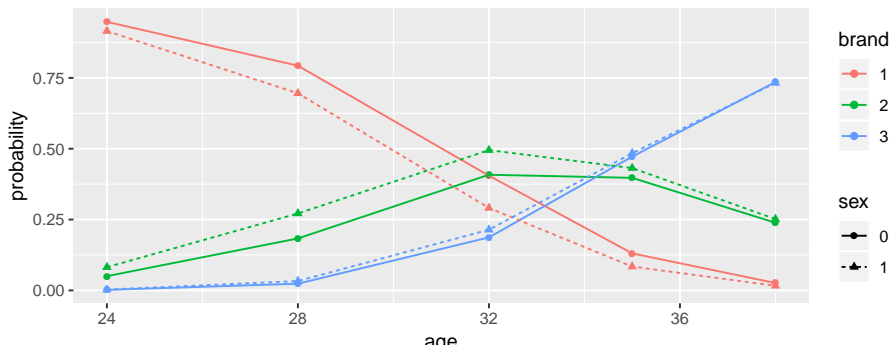
The tidy data (random sample of rows)

```
probs.long %>% sample_n(10)
```

```
## # A tibble: 10 x 4
##       age sex  brand probability
##   <dbl> <fct> <chr>      <dbl>
## 1    28  0     1        0.793
## 2    32  0     1        0.405
## 3    38  0     1        0.0260
## 4    24  1     2        0.0819
## 5    32  1     3        0.214
## 6    35  1     3        0.484
## 7    24  1     1        0.915
## 8    35  0     3        0.472
## 9    35  1     1        0.0840
## 10   32  0     2        0.408
```

The plot

```
ggplot(probs.long, aes(
  x = age, y = probability,
  colour = brand, shape = sex
)) +
  geom_point() + geom_line(aes(linetype = sex))
```



Digesting the plot

- Brand vs. age: younger people (of both genders) prefer brand 1, but older people (of both genders) prefer brand 3. (Explains significant age effect.)
- Brand vs. sex: females (dashed) like brand 1 less than males (solid), like brand 2 more (for all ages).
- Not much brand difference between genders (solid and dashed lines of same colours close), but enough to be significant.
- Model didn't include interaction, so modelled effect of gender on brand same for each age, modelled effect of age same for each gender.

Alternative data format

Summarize all people of same brand preference, same sex, same age on one line of data file with frequency on end:

1 0 24 1

1 0 26 2

1 0 27 4

1 0 28 4

1 0 29 7

1 0 30 3

...

Whole data set in 65 lines not 735! But how?

Getting alternative data format

```
brandpref %>%
  group_by(age, sex, brand) %>%
  summarize(Freq = n()) %>%
  ungroup() -> b
b %>% slice(1:6)
```

```
## # A tibble: 6 x 4
##   age sex  brand  Freq
##   <dbl> <fct> <fct> <int>
## 1    24 0     1      1
## 2    26 0     1      2
## 3    27 0     1      4
## 4    27 1     1      4
## 5    27 1     3      1
## 6    28 0     1      4
```

Fitting models, almost the same

- Just have to remember weights to incorporate frequencies.
- Otherwise multinom assumes you have just 1 obs on each line!
- Again turn (numerical) sex and brand into factors:

```
b %>%
  mutate(sex = factor(sex)) %>%
  mutate(brand = factor(brand)) -> bf
b.1 <- multinom(brand ~ age + sex, data = bf, weights = Freq)
b.2 <- multinom(brand ~ age, data = bf, weights = Freq)
```


P-value for sex identical

```
anova(b.2, b.1)
```

```
## Likelihood ratio tests of Multinomial Models
```

```
##
```

```
## Response: brand
```

##	Model	Resid. df	Resid. Dev	Test	Df	LR stat.	Pr(Chi)
## 1	age	126	1413.593				
## 2	age + sex	124	1405.941	1 vs 2	2	7.651236	0.02180495

Same P-value as before, so we haven't changed anything important.

Including data on plot

- Everyone's age given as whole number, so maybe not too many different ages with sensible amount of data at each:

```
b %>%
  group_by(age) %>%
  summarize(total = sum(Freq))
```

```
## # A tibble: 14 x 2
##   age total
##   <dbl> <int>
## 1     24     1
## 2     26     2
## 3     27     9
## 4     28    15
## 5     29    19
## 6     30    23
## 7     31    40
## 8     32   333
## 9     33    55
## 10    34    64
## 11    35    35
## 12    36    85
## 13    37    22
```

Comments and next

- Not great (especially at low end), but live with it.
- Need proportions of frequencies in each brand for each age-gender combination. Mimic what we did for miners:

```
b %>%  
  group_by(age, sex) %>%  
  mutate(proportion = Freq / sum(Freq)) -> brands
```

Checking proportions for age 32

```
brands %>% filter(age == 32)
```

```
## # A tibble: 6 x 5
## # Groups:   age, sex [2]
##   age sex  brand  Freq proportion
##   <dbl> <fct> <fct> <int>      <dbl>
## 1    32 0     1      48      0.407
## 2    32 0     2      51      0.432
## 3    32 0     3      19      0.161
## 4    32 1     1      62      0.288
## 5    32 1     2     117      0.544
## 6    32 1     3      36      0.167
```

- First three proportions (males) add up to 1.
- Last three proportions (females) add up to 1.
- So looks like proportions of right thing.

Attempting plot

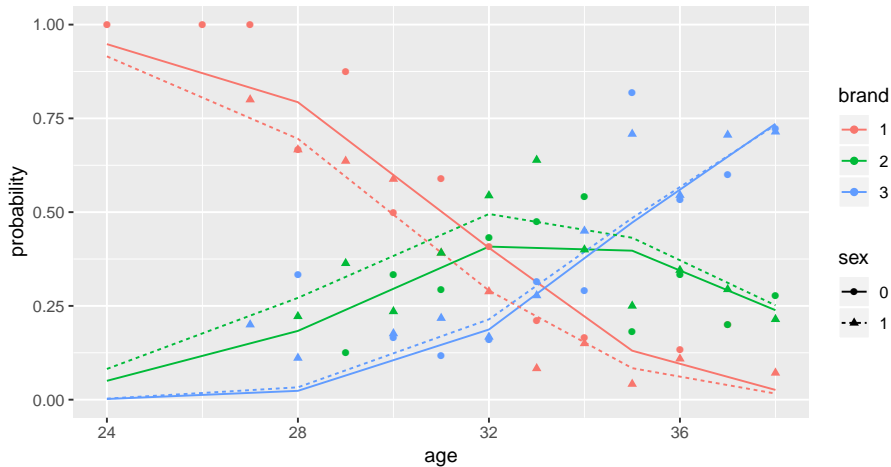
- Take code from previous plot and:
- remove `geom_point` for fitted values
- add `geom_point` with correct `data=` and `aes` to plot data.

```
g <- ggplot(probs.long, aes(
  x = age, y = probability,
  colour = brand, shape = sex
)) +
  geom_line(aes(linetype = sex)) +
  geom_point(data = brands, aes(y = proportion))
```

- Data seem to correspond more or less to fitted curves:

The plot

g



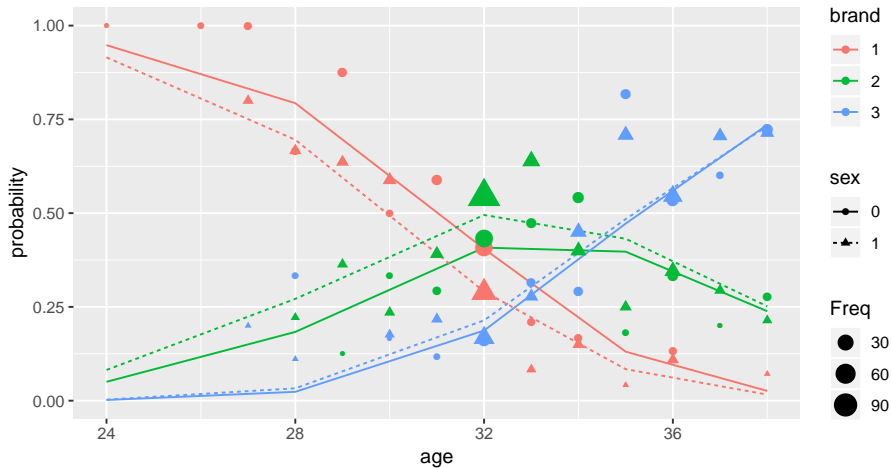
But...

- Some of the plotted points based on a lot of people, and some only a few.
- Idea: make the *size* of plotted point bigger if point based on a lot of people (in Freq).
- Hope that larger points then closer to predictions.
- Code:

```
g <- ggplot(probs.long, aes(
  x = age, y = probability,
  colour = brand, shape = sex
)) +
  geom_line(aes(linetype = sex)) +
  geom_point(
    data = brands,
    aes(y = proportion, size = Freq)
  )
```

The plot

g



Trying interaction between age and gender

```
b.4 <- update(b.1, . ~ . + age:sex)
```

```
## # weights: 15 (8 variable)
## initial value 807.480032
## iter 10 value 704.811229
## iter 20 value 702.582802
## final value 702.582761
## converged
```

```
anova(b.1, b.4)
```

```
## Likelihood ratio tests of Multinomial Models
```

```
##
```

```
## Response: brand
```

##	Model	Resid. df	Resid. Dev	Test	Df
## 1	age + sex	124	1405.941		
## 2	age + sex + age:sex	122	1405.166	1 vs 2	2

```
## LR stat. Pr(Chi)
```

## 1	
## 2	0.7758861 0.678451

- No evidence that effect of age on brand preference differs for the two genders.

Section 4

Survival analysis

Survival analysis

- So far, have seen:
 - response variable counted or measured (regression)
 - response variable categorized (logistic regression)

and have predicted response from explanatory variables.

- But what if response is time until event (eg. time of survival after surgery)?
- Additional complication: event might not have happened at end of study (eg. patient still alive). But knowing that patient has “not died yet” presumably informative. Such data called *censored*.
- Enter *survival analysis*, in particular the “Cox proportional hazards model”.
- Explanatory variables in this context often called *covariates*.

Example: still dancing?

- 12 women who have just started taking dancing lessons are followed for up to a year, to see whether they are still taking dancing lessons, or have quit. The “event” here is “quit”.
- This might depend on:
 - a treatment (visit to a dance competition)
 - woman's age (at start of study).

Data

Months	Quit	Treatment	Age
1	1	0	16
2	1	0	24
2	1	0	18
3	0	0	27
4	1	0	25
7	1	1	26
8	1	1	36
10	1	1	38
10	0	1	45
12	1	1	47

About the data

- `months` and `quit` are kind of combined response:
 - `Months` is number of months a woman was actually observed dancing
 - `quit` is 1 if woman quit, 0 if still dancing at end of study.
- `Treatment` is 1 if woman went to dance competition, 0 otherwise.
- Fit model and see whether `Age` or `Treatment` have effect on survival.
- Want to do predictions for probabilities of still dancing as they depend on whatever is significant, and draw plot.

Packages (for this section)

- Install packages `survival` and `survminer` if not done.
- Load `survival`, `survminer`, `broom` and `tidyverse`:

```
library(tidyverse)
library(survival)
library(survminer)
library(broom)
```

Read data

- Column-aligned:

```
url <- "http://www.utsc.utoronto.ca/~butler/d29/dancing.txt"
dance <- read_table(url)
```

```
## Parsed with column specification:
## cols(
##   Months = col_double(),
##   Quit = col_double(),
##   Treatment = col_double(),
##   Age = col_double()
## )
```


The data

```
dance
```

```
## # A tibble: 12 x 4
##   Months  Quit Treatment   Age
##   <dbl> <dbl>      <dbl> <dbl>
## 1      1      1          0     16
## 2      2      1          0     24
## 3      2      1          0     18
## 4      3      0          0     27
## 5      4      1          0     25
## 6      5      1          0     21
## 7     11      1          0     55
## 8      7      1          1     26
## 9      8      1          1     36
## 10     10      1          1     38
## 11     10      0          1     45
## 12     12      1          1     47
```

Examine response and fit model

- Response variable (has to be outside data frame):

```
mth <- with(dance, Surv(Months, Quit))
mth
```

```
## [1] 1 2 2 3+ 4 5 11 7 8 10 10+ 12
```

- Then fit model, predicting `mth` from explanatories:

```
dance.1 <- coxph(mth ~ Treatment + Age, data = dance)
```

Output looks a lot like regression

```
summary(dance.1)
```

```
## Call:
## coxph(formula = mth ~ Treatment + Age, data = dance)
##
## n= 12, number of events= 10
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## Treatment -4.44915   0.01169  2.60929 -1.705   0.0882 .
## Age       -0.36619   0.69337  0.15381 -2.381   0.0173 *
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## Treatment    0.01169    85.554 7.026e-05    1.9444
## Age          0.69337     1.442 5.129e-01    0.9373
##
## Concordance= 0.964 (se = 0.039 )
## Likelihood ratio test= 21.68  on 2 df,   p=2e-05
## Wald test            = 5.67  on 2 df,   p=0.06
## Score (logrank) test = 14.75  on 2 df,   p=6e-04
```

Conclusions

- Use $\alpha = 0.10$ here since not much data.
- Three tests at bottom like global F-test. Consensus that something predicts survival time (whether or not dancer quit and how long it took).
- Age (definitely), Treatment (marginally) both predict survival time.

Model checking

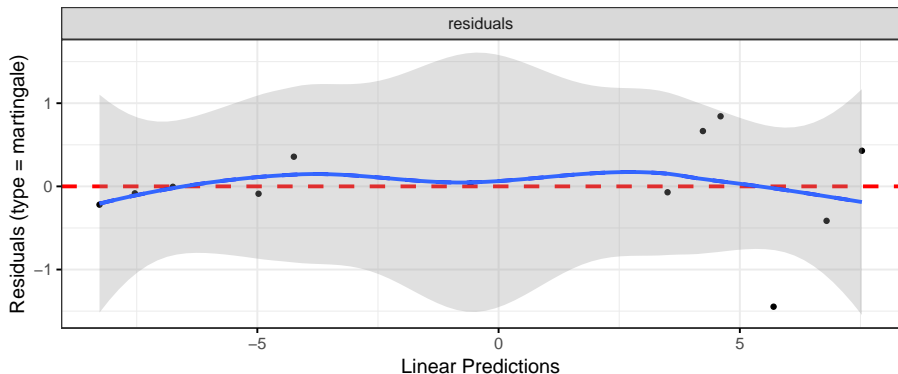
- With regression, usually plot residuals against fitted values.
- Not quite same here (nonlinear model), but “martingale residuals” should have no pattern vs. “linear predictor”.
- `ggcoxdiagnostics` from package `survminer` makes plot, to which we add smooth. If smooth trend more or less straight across, model OK.
- Martingale residuals can go very negative, so won't always look normal.

Martingale residual plot for dance data

This looks good (with only 12 points):

```
ggcoxdiagnostics(dance.1) + geom_smooth(se = F)
```

```
## `geom_smooth()` using method = 'loess' and formula 'y ~ x'
```



Predicted survival probs

- The function we use is called `survfit`, though actually works rather like `predict`.
- First create a data frame of values to predict from. We'll do all combos of ages 20 and 40, treatment and not, using `crossing` to get all the combos:

```
treatments <- c(0, 1)
ages <- c(20, 40)
dance.new <- crossing(Treatment = treatments, Age = ages)
dance.new
```

```
## # A tibble: 4 x 2
##   Treatment    Age
##   <dbl> <dbl>
## 1         0     20
## 2         0     40
## 3         1     20
## 4         1     40
```

The predictions

One prediction *for each time* for each combo of age and treatment in `dance.new`:

```
s <- survfit(dance.1, newdata = dance.new, data = dance)
summary(s)
```

```
## Call: survfit(formula = dance.1, newdata = dance.new, data = dance)
##
##   time  n.risk  n.event survival1 survival2 survival3 survival4
##    1      12        1  8.76e-01  1.00e+00  9.98e-01    1.000
##    2      11        2  3.99e-01  9.99e-01  9.89e-01    1.000
##    4       8        1  1.24e-01  9.99e-01  9.76e-01    1.000
##    5       7        1  2.93e-02  9.98e-01  9.60e-01    1.000
##    7       6        1 2.96e-323  6.13e-01  1.70e-04    0.994
##    8       5        1  0.00e+00  2.99e-06  1.35e-98    0.862
##   10       4        1  0.00e+00  3.61e-20  0.00e+00    0.593
##   11       2        1  0.00e+00  0.00e+00  0.00e+00    0.000
##   12       1        1  0.00e+00  0.00e+00  0.00e+00    0.000
```


Conclusions from predicted probs

- Older women more likely to be still dancing than younger women (compare “profiles” for same treatment group).
- Effect of treatment seems to be to increase prob of still dancing (compare “profiles” for same age for treatment group vs. not)
- Would be nice to see this on a graph. This is `ggsurvplot` from package `survminer`:

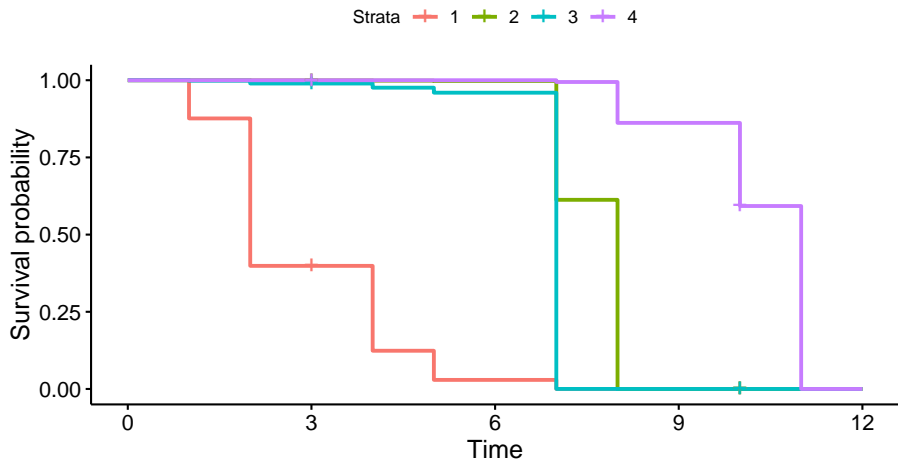
```
g <- ggsurvplot(s, conf.int = F)
```

- uses “strata” thus (`dance.new`):

```
## # A tibble: 4 x 2
##   Treatment Age
##       <dbl> <dbl>
## 1         0    20
## 2         0    40
## 3         1    20
## 4         1    40
```

Plotting survival probabilities

g



Discussion

- Survivor curve farther to the right is better (better chance of surviving longer).
- Best is age 40 with treatment, worst age 20 without.
- Appears to be:
 - age effect (40 better than 20)
 - treatment effect (treatment better than not)
 - In analysis, treatment effect only marginally significant.

A more realistic example: lung cancer

- When you load in an R package, get data sets to illustrate functions in the package.
- One such is `lung`. Data set measuring survival in patients with advanced lung cancer.
- Along with survival time, number of “performance scores” included, measuring how well patients can perform daily activities.
- Sometimes high good, but sometimes bad!
- Variables below, from the data set help file (`?lung`).

The variables

Format

inst: Institution code
time: Survival time in days
status: censoring status 1=censored, 2=dead
age: Age in years
sex: Male=1 Female=2
ph.ecog: ECOG performance score (0=good 5=dead)
ph.karno: Karnofsky performance score (bad=0-good=100) rated by physician
pat.karno: Karnofsky performance score as rated by patient
meal.cal: Calories consumed at meals
wt.loss: Weight loss in last six months

Uh oh, missing values

```
lung %>% slice(1:16)
```

##	inst	time	status	age	sex	ph.ecog	ph.karno	pat.karno	meal.cal	wt.loss
## 1	3	306	2	74	1	1	90	100	1175	NA
## 2	3	455	2	68	1	0	90	90	1225	15
## 3	3	1010	1	56	1	0	90	90	NA	15
## 4	5	210	2	57	1	1	90	60	1150	11
## 5	1	883	2	60	1	0	100	90	NA	0
## 6	12	1022	1	74	1	1	50	80	513	0
## 7	7	310	2	68	2	2	70	60	384	10
## 8	11	361	2	71	2	2	60	80	538	1
## 9	1	218	2	53	1	1	70	80	825	16
## 10	7	166	2	61	1	2	70	70	271	34
## 11	6	170	2	57	1	1	80	80	1025	27
## 12	16	654	2	68	2	2	70	70	NA	23
## 13	11	728	2	68	2	1	90	90	NA	5
## 14	21	71	2	60	1	NA	60	70	1225	32
## 15	12	567	2	57	1	1	80	70	2600	60
## 16	1	144	2	67	1	1	80	90	NA	15

A closer look

```
summary(lung)
```

```
##      inst      time      status      age      sex
## Min.   : 1.00   Min.    : 5.0   Min.    :1.000   Min.    :39.00   Min.    :1.000
## 1st Qu.: 3.00   1st Qu.: 166.8   1st Qu.:1.000   1st Qu.:56.00   1st Qu.:1.000
## Median :11.00   Median : 255.5   Median :2.000   Median :63.00   Median :1.000
## Mean   :11.09   Mean    : 305.2   Mean    :1.724   Mean    :62.45   Mean    :1.395
## 3rd Qu.:16.00   3rd Qu.: 396.5   3rd Qu.:2.000   3rd Qu.:69.00   3rd Qu.:2.000
## Max.   :33.00   Max.    :1022.0   Max.    :2.000   Max.    :82.00   Max.    :2.000
## NA's    :1
##      ph.ecog      ph.karno      pat.karno      meal.cal      wt.loss
## Min.   :0.0000   Min.    : 50.00   Min.    : 30.00   Min.    : 96.0   Min.    :~24.000
## 1st Qu.:0.0000   1st Qu.: 75.00   1st Qu.: 70.00   1st Qu.: 635.0   1st Qu.: 0.000
## Median :1.0000   Median : 80.00   Median : 80.00   Median : 975.0   Median : 7.000
## Mean   :0.9515   Mean    : 81.94   Mean    : 79.96   Mean    : 928.8   Mean    : 9.832
## 3rd Qu.:1.0000   3rd Qu.: 90.00   3rd Qu.: 90.00   3rd Qu.:1150.0   3rd Qu.: 15.750
## Max.   :3.0000   Max.    :100.00   Max.    :100.00   Max.    :2600.0   Max.    : 68.000
## NA's    :1      NA's    :1      NA's    :3      NA's    :47      NA's    :14
```

Remove obs with *any* missing values

```
lung %>% drop_na() -> lung.complete
lung.complete %>%
  select(meal.cal:wt.loss) %>%
  slice(1:10)
```

##	meal.cal	wt.loss
## 1	1225	15
## 2	1150	11
## 3	513	0
## 4	384	10
## 5	538	1
## 6	825	16
## 7	271	34
## 8	1025	27
## 9	2600	60
## 10	1150	-5

Missing values seem to be gone.

Check!

```
summary(lung.complete)
```

```
##          inst           time           status           age           sex
## Min.      : 1.00    Min.      : 5.0    Min.      :1.000    Min.      :39.00    Min.      :1.000
## 1st Qu.: 3.00    1st Qu.: 174.5    1st Qu.:1.000    1st Qu.:57.00    1st Qu.:1.000
## Median :11.00    Median : 268.0    Median :2.000    Median :64.00    Median :1.000
## Mean   :10.71    Mean   : 309.9    Mean   :1.719    Mean   :62.57    Mean   :1.383
## 3rd Qu.:15.00    3rd Qu.: 419.5    3rd Qu.:2.000    3rd Qu.:70.00    3rd Qu.:2.000
## Max.    :32.00    Max.    :1022.0    Max.    :2.000    Max.    :82.00    Max.    :2.000
##   ph.ecog   ph.karno   pat.karno   meal.cal   wt.loss
## Min.      :0.0000    Min.      : 50.00    Min.      : 30.00    Min.      : 96.0    Min.      : -24.000
## 1st Qu.:0.0000    1st Qu.: 70.00    1st Qu.: 70.00    1st Qu.: 619.0    1st Qu.: 0.000
## Median :1.0000    Median : 80.00    Median : 80.00    Median : 975.0    Median : 7.000
## Mean   :0.9581    Mean   : 82.04    Mean   : 79.58    Mean   : 929.1    Mean   : 9.719
## 3rd Qu.:1.0000    3rd Qu.: 90.00    3rd Qu.: 90.00    3rd Qu.:1162.5    3rd Qu.: 15.000
## Max.    :3.0000    Max.    :100.00    Max.    :100.00    Max.    :2600.0    Max.    : 68.000
```

No missing values left.

Model 1: use everything except inst

```
names(lung.complete)
```

```
## [1] "inst"      "time"      "status"    "age"       "sex"       "ph.eco"
## [8] "pat.karno" "meal.cal"  "wt.loss"
```

- Event was death, goes with status of 2:

```
resp <- with(lung.complete, Surv(time, status == 2))
lung.1 <- coxph(resp ~ . - inst - time - status,
  data = lung.complete
)
```

“Dot” means “all the other variables”.

summary of model 1: too tiny to see!

```
summary(lung.1)
```

```
## Call:
## coxph(formula = resp ~ . - inst - time - status, data = lung.complete)
##
## n= 167, number of events= 120
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## age           1.080e-02  1.011e+00  1.160e-02  0.931  0.35168
## sex           -5.536e-01  5.749e-01  2.016e-01 -2.746  0.00603 **
## ph.ecog        7.395e-01  2.095e+00  2.250e-01  3.287  0.00101 **
## ph.karno       2.244e-02  1.023e+00  1.123e-02  1.998  0.04575 *
## pat.karno     -1.207e-02  9.880e-01  8.116e-03 -1.488  0.13685
## meal.cal       2.835e-05  1.000e+00  2.594e-04  0.109  0.91298
## wt.loss       -1.420e-02  9.859e-01  7.766e-03 -1.828  0.06748 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## age           1.0109      0.9893    0.9881    1.0341
## sex           0.5749      1.7395    0.3872    0.8534
## ph.ecog        2.0950      0.4773    1.3479    3.2560
## ph.karno       1.0227      0.9778    1.0004    1.0455
## pat.karno      0.9880      1.0121    0.9724    1.0038
## meal.cal       1.0000      1.0000    0.9995    1.0005
## wt.loss        0.9859      1.0143    0.9710    1.0010
##
## Concordance= 0.653 (se = 0.029 )
## Likelihood ratio test= 28.16 on 7 df,  p=2e-04
## Wald test              = 27.5 on 7 df,  p=3e-04
## Score (logrank) test = 28.31 on 7 df,  p=2e-04
```

Overall significance

The three tests of overall significance:

```
glance(lung.1) %>% select(starts_with("p.value"))
```

```
## # A tibble: 1 x 3
##   p.value.log p.value.sc p.value.wald
##         <dbl>         <dbl>         <dbl>
## 1    0.000205    0.000193    0.000271
```

All strongly significant. *Something* predicts survival.

Coefficients for model 1

```
tidy(lung.1) %>% select(term, p.value) %>% arrange(p.value)
```

```
## # A tibble: 7 x 2
##   term      p.value
##   <chr>      <dbl>
## 1 ph.ecog  0.00101
## 2 sex      0.00603
## 3 ph.karno 0.0457
## 4 wt.loss  0.0675
## 5 pat.karno 0.137
## 6 age      0.352
## 7 meal.cal 0.913
```

- sex and ph.ecog definitely significant here
- age, pat.karno and meal.cal definitely not
- Take out definitely non-sig variables, and try again.

Model 2

```
lung.2 <- update(lung.1, . ~ . - age - pat.karno - meal.cal)
tidy(lung.2) %>% select(term, p.value)
```

```
## # A tibble: 4 x 2
##   term      p.value
##   <chr>      <dbl>
## 1 sex        0.00409
## 2 ph.ecog    0.000112
## 3 ph.karno   0.101
## 4 wt.loss    0.108
```

Compare with first model:

```
anova(lung.2, lung.1)
```

```
## Analysis of Deviance Table
##   Cox model: response is  resp
##   Model 1: ~ sex + ph.ecog + ph.karno + wt.loss
##   Model 2: ~ (inst + time + status + age + sex + ph.ecog + p
##      loglik Chisq Df P(>|Chi|)
## 1 -495.67
## 2 -494.03 3.269 3      0.352
```

- No harm in taking out those variables.

Model 3

Take out ph.karno and wt.loss as well.

```
lung.3 <- update(lung.2, . ~ . - ph.karno - wt.loss)
```

```
tidy(lung.3) %>% select(term, estimate, p.value)
```

```
## # A tibble: 2 x 3
##   term      estimate p.value
##   <chr>      <dbl>    <dbl>
## 1 sex        -0.510  0.00958
## 2 ph.ecog     0.483  0.000266
```


Check whether that was OK

```
anova(lung.3, lung.2)
```

```
## Analysis of Deviance Table
##   Cox model: response is  resp
##   Model 1: ~ sex + ph.ecog
##   Model 2: ~ sex + ph.ecog + ph.karno + wt.loss
##      loglik   Chisq Df P(>|Chi|)
## 1 -498.38
## 2 -495.67  5.4135   2   0.06675 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Just OK.

Commentary

- OK (just) to take out those two covariates.
- Both remaining variables strongly significant.
- Nature of effect on survival time? Consider later.
- Picture?

Plotting survival probabilities

- Create new data frame of values to predict for, then predict:

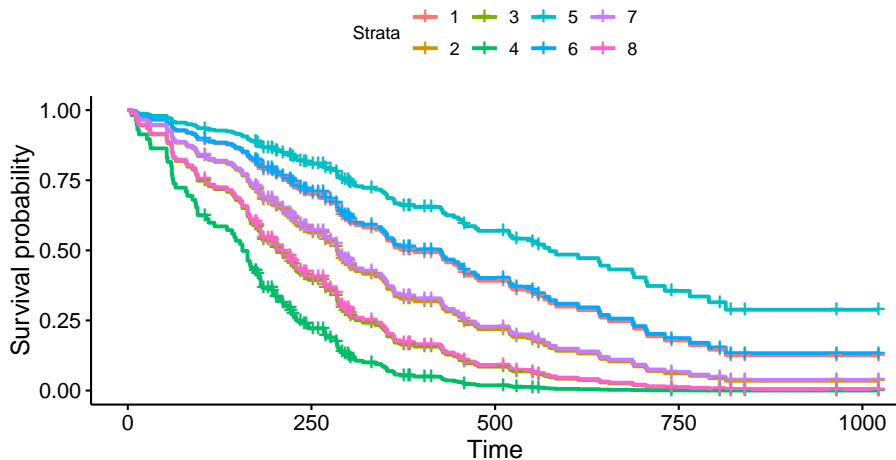
```
sexes <- c(1, 2)
ph.ecogs <- 0:3
lung.new <- crossing(sex = sexes, ph.ecog = ph.ecogs)
lung.new
```

```
## # A tibble: 8 x 2
##       sex ph.ecog
##   <dbl>   <int>
## 1     1     0
## 2     1     1
## 3     1     2
## 4     1     3
## 5     2     0
## 6     2     1
## 7     2     2
## 8     2     3
```

```
s <- survfit(lung.3, data = lung.complete, newdata = lung.new)
```

The plot

```
ggsurvplot(s, conf.int = F)
```



Discussion of survival curves

- Best survival is teal-blue curve, stratum 5, females with (ph.ecog) score 0.
- Next best: blue, stratum 6, females with score 1, and red, stratum 1, males score 0.
- Worst: green, stratum 4, males score 3.
- For any given ph.ecog score, females have better predicted survival than males.
- For both genders, a lower score associated with better survival.

The coefficients in model 3

```
tidy(lung.3) %>% select(term, estimate, p.value)
```

```
## # A tibble: 2 x 3
##   term      estimate p.value
##   <chr>      <dbl>    <dbl>
## 1 sex        -0.510  0.00958
## 2 ph.ecog     0.483  0.000266
```

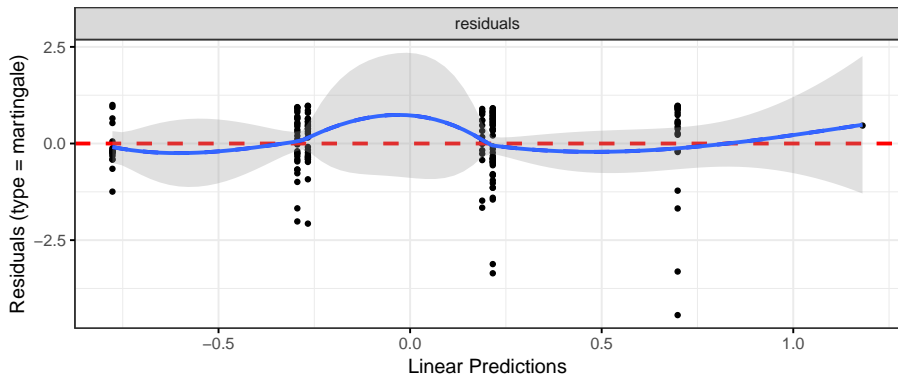
- sex coeff negative, so being higher sex value (female) goes with *less* hazard of dying.
- ph.ecog coeff positive, so higher ph.ecog score goes with *more* hazard of dying
- Two coeffs about same size, so being male rather than female corresponds to 1-point increase in ph.ecog score. Note how survival curves come in 3 pairs plus 2 odd.

Martingale residuals for this model

No problems here:

```
ggcoxdiagnostics(lung.3) + geom_smooth(se = F)
```

```
## `geom_smooth()` using method = 'loess' and formula 'y ~ x'
```



When the Cox model fails

- Invent some data where survival is best at middling age, and worse at high *and* low age:

```
age <- seq(20, 60, 5)
survtime <- c(10, 12, 11, 21, 15, 20, 8, 9, 11)
stat <- c(1, 1, 1, 1, 0, 1, 1, 1, 1)
d <- tibble(age, survtime, stat)
y <- with(d, Surv(survtime, stat))
```

- Small survival time 15 in middle was actually censored, so would have been longer if observed.

Fit Cox model

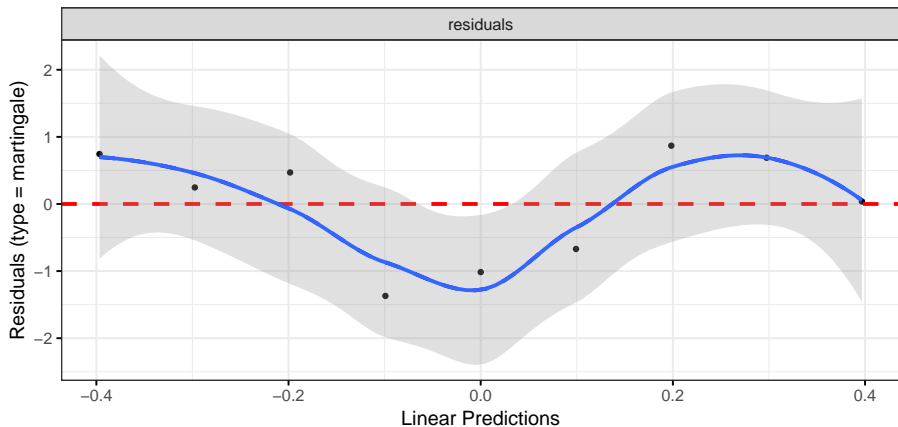
```
y.1 <- coxph(y ~ age, data = d)
summary(y.1)
```

```
## Call:
## coxph(formula = y ~ age, data = d)
##
##      n= 9, number of events= 8
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## age 0.01984      1.02003  0.03446 0.576    0.565
##
##      exp(coef) exp(-coef) lower .95 upper .95
## age          1.02      0.9804    0.9534    1.091
##
## Concordance= 0.545  (se = 0.105 )
## Likelihood ratio test= 0.33  on 1 df,   p=0.6
## Wald test               = 0.33  on 1 df,   p=0.6
## Score (logrank) test = 0.33  on 1 df,   p=0.6
```

Martingale residuals

Down-and-up indicates incorrect relationship between age and survival:

```
ggcoxdiagnostics(y.1) + geom_smooth(se = F)
```



Attempt 2

Add squared term in age:

```
y.2 <- coxph(y ~ age + I(age^2), data = d)
tidy(y.2) %>% select(term, estimate, p.value)
```

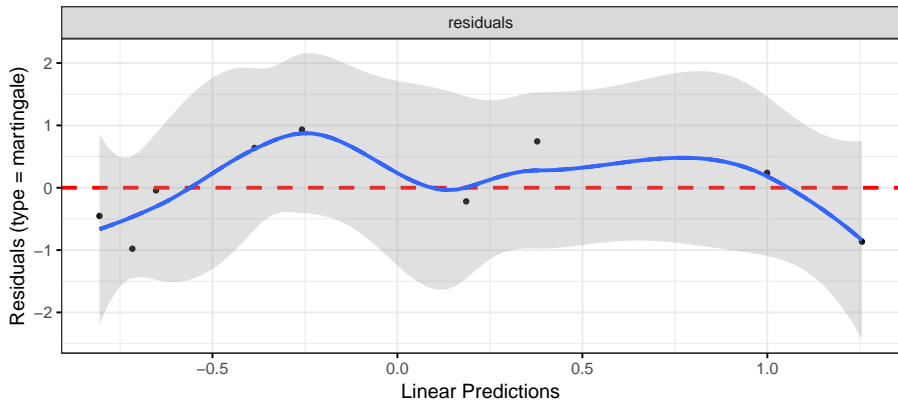
```
## # A tibble: 2 x 3
##   term      estimate p.value
##   <chr>      <dbl>    <dbl>
## 1 age      -0.380      0.116
## 2 I(age^2)  0.00483     0.0977
```

- (Marginally) helpful.

Martingale residuals this time

Not great, but less problematic than before:

```
ggcoxdiagnostics(y.2) + geom_smooth(se = F)
```



Section 5

Analysis of variance

Analysis of variance

- Analysis of variance used with:
 - counted/measured response
 - categorical explanatory variable(s)
 - that is, data divided into groups, and see if response significantly different among groups
 - or, see whether knowing group membership helps to predict response.
- Typically two stages:
 - F -test to detect *any* differences among/due to groups
 - if F -test significant, do *multiple comparisons* to see which groups significantly different from which.
- Need special multiple comparisons method because just doing (say) two-sample t -tests on each pair of groups gives too big a chance of finding “significant” differences by accident.

Packages

These:

```
library(tidyverse)
library(broom)
library(car) # for Levene's test
```

Example: Pain threshold and hair colour

- Do people with different hair colour have different abilities to deal with pain?
- Men and women of various ages divided into 4 groups by hair colour: light and dark blond, light and dark brown.
- Each subject given a pain sensitivity test resulting in pain threshold score: higher score is higher pain tolerance.
- 19 subjects altogether.

The data

In hairpain.txt:

hair pain	darkblond 43
lightblond 62	lightbrown 42
lightblond 60	lightbrown 50
lightblond 71	lightbrown 41
lightblond 55	lightbrown 37
lightblond 48	darkbrown 32
darkblond 63	darkbrown 39
darkblond 57	darkbrown 51
darkblond 52	darkbrown 30
darkblond 41	darkbrown 35

Summarizing the groups

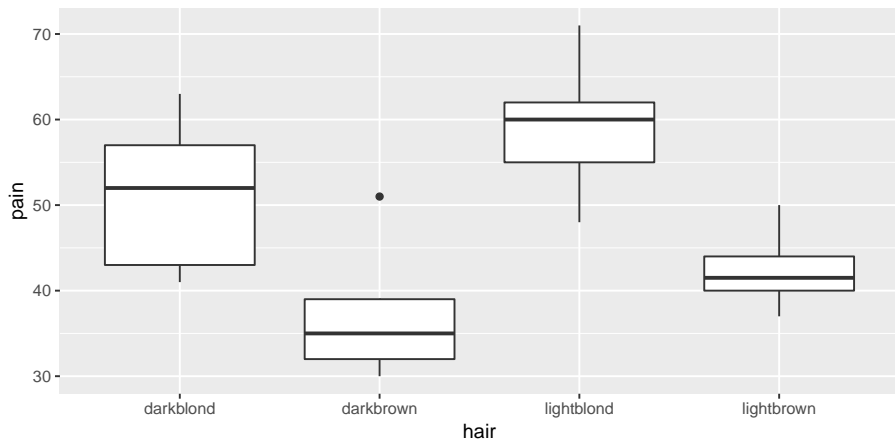
```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/hairpain.txt"
hairpain <- read_delim(my_url, " ")
hairpain %>%
  group_by(hair) %>%
  summarize(
    n = n(),
    xbar = mean(pain),
    s = sd(pain)
  )
```

```
## # A tibble: 4 x 4
##   hair      n  xbar    s
##   <chr>  <int> <dbl> <dbl>
## 1 darkblond    5  51.2  9.28
## 2 darkbrown    5  37.4  8.32
## 3 lightblond    5  59.2  8.53
## 4 lightbrown    4  42.5  5.45
```

Brown-haired people seem to have lower pain tolerance.

Boxplot

```
ggplot(hairpain, aes(x = hair, y = pain)) + geom_boxplot()
```



Assumptions

- Data should be:
 - normally distributed within each group
 - same spread for each group
- darkbrown group has upper outlier (suggests not normal)
- darkblond group has smaller IQR than other groups.
- But, groups *small*.
- Shrug shoulders and continue for moment.

Testing equality of SDs

- via **Levene's test** in package `car`:

```
leveneTest(pain ~ hair, data = hairpain)
```

```
## Warning in leveneTest.default(y = y, group = group, ...): group
```

```
## Levene's Test for Homogeneity of Variance (center = median)
```

```
##           Df F value Pr(>F)
```

```
## group    3  0.3927  0.76
```

```
##           15
```

- No evidence (at all) of difference among group SDs.
- Possibly because groups *small*.

Analysis of variance

```
hairpain.1 <- aov(pain ~ hair, data = hairpain)
summary(hairpain.1)
```

```
##              Df Sum Sq Mean Sq F value Pr(>F)
## hair          3   1361    453.6    6.791 0.00411 **
## Residuals    15   1002     66.8
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- P-value small: the mean pain tolerances for the four groups are *not* all the same.
- Which groups differ from which, and how?

Multiple comparisons

- Which groups differ from which? Multiple comparisons method. Lots.
- Problem: by comparing all the groups with each other, doing many tests, have large chance to (possibly incorrectly) reject H_0 : groups have equal means.
- 4 groups: 6 comparisons (1 vs 2, 1 vs 3, ..., 3 vs 4). 5 groups: 10 comparisons. Thus 6 (or 10) chances to make mistake.
- Get “familywise error rate” of 0.05 (whatever), no matter how many comparisons you’re doing.
- My favourite: Tukey, or “honestly significant differences”: how far apart might largest, smallest group means be (if actually no differences). Group means more different: significantly different.

Tukey

- TukeyHSD:

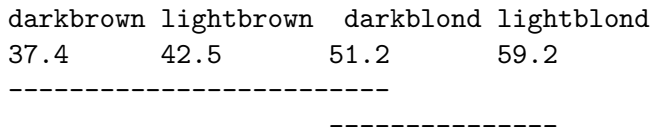
```
TukeyHSD(hairpain.1)
```

```
##      Tukey multiple comparisons of means
##      95% family-wise confidence level
##
## Fit: aov(formula = pain ~ hair, data = hairpain)
##
## $hair
```

	diff	lwr	upr	p adj
darkbrown-darkblond	-13.8	-28.696741	1.0967407	0.0740679
lightblond-darkblond	8.0	-6.896741	22.8967407	0.4355768
lightbrown-darkblond	-8.7	-24.500380	7.1003795	0.4147283
lightblond-darkbrown	21.8	6.903259	36.6967407	0.0037079
lightbrown-darkbrown	5.1	-10.700380	20.9003795	0.7893211
lightbrown-lightblond	-16.7	-32.500380	-0.8996205	0.0366467

The old-fashioned way

- List group means in order
- Draw lines connecting groups that are *not* significantly different:



- lightblond significantly higher than everything except darkblond (at $\alpha = 0.05$).
- darkblond in middle ground: not significantly less than lightblond, not significantly greater than darkbrown and lightbrown.
- More data might resolve this.
- Looks as if blond-haired people do have higher pain tolerance, but not completely clear.

Some other multiple-comparison methods

- Work any time you do k tests at once (not just ANOVA).
 - **Bonferroni**: multiply all P-values by k .
 - **Holm**: multiply smallest P-value by k , next-smallest by $k - 1$, etc.
 - **False discovery rate**: multiply smallest P-value by $k/1$, 2nd-smallest by $k/2$, ..., i -th smallest by k/i .
- Stop after non-rejection.

Example

- P-values 0.005, 0.015, 0.03, 0.06 (4 tests all done at once) Use $\alpha = 0.05$.
- Bonferroni:
 - Multiply all P-values by 4 (4 tests).
 - Reject only 1st null.
- Holm:
 - Times smallest P-value by 4: $0.005 * 4 = 0.020 < 0.05$, reject.
 - Times next smallest by 3: $0.015 * 3 = 0.045 < 0.05$, reject.
 - Times next smallest by 2: $0.03 * 2 = 0.06 > 0.05$, do not reject. Stop.

...Continued

- With P-values 0.005, 0.015, 0.03, 0.06:
- False discovery rate:
 - Times smallest P-value by 4: $0.005 * 4 = 0.02 < 0.05$: reject.
 - Times second smallest by $4/2$: $0.015 * 4/2 = 0.03 < 0.05$, reject.
 - Times third smallest by $4/3$: $0.03 * 4/3 = 0.04 < 0.05$, reject.
 - Times fourth smallest by $4/4$: $0.06 * 4/4 = 0.06 > 0.05$, do not reject.
Stop.

pairwise.t.test

```
attach(hairpain)
pairwise.t.test(pain, hair, p.adj = "none")

##
## Pairwise comparisons using t tests with pooled SD
##
## data:  pain and hair
##
##           darkblond darkbrown lightblond
## darkbrown  0.01748   -             -
## lightblond 0.14251   0.00075   -
## lightbrown 0.13337   0.36695   0.00817
##
## P value adjustment method: none
pairwise.t.test(pain, hair, p.adj = "holm")
```

```
##
## Pairwise comparisons using t tests with pooled SD
##
## data:  pain and hair
##
##           darkblond darkbrown lightblond
## darkbrown  0.0699   -             -
## lightblond 0.4001   0.0045   -
## lightbrown 0.4001   0.4001   0.0408
##
## P value adjustment method: holm
```

pairwise.t.test part 2

```
pairwise.t.test(pain, hair, p.adj = "fdr")
```

```
##
## Pairwise comparisons using t tests with pooled SD
##
## data:  pain and hair
##
##           darkblond darkbrown lightblond
## darkbrown  0.0350    -            -
## lightblond 0.1710    0.0045    -
## lightbrown 0.1710    0.3670    0.0245
##
## P value adjustment method: fdr
```

```
pairwise.t.test(pain, hair, p.adj = "bon")
```

```
##
## Pairwise comparisons using t tests with pooled SD
##
## data:  pain and hair
##
##           darkblond darkbrown lightblond
## darkbrown  0.1049    -            -
## lightblond 0.8550    0.0045    -
## lightbrown 0.8002    1.0000    0.0490
##
## P value adjustment method: bonferroni
```

Comments

- P-values all adjusted upwards from “none”.
- Required because 6 tests at once.
- Highest P-values for Bonferroni: most “conservative”.
- Prefer Tukey or FDR or Holm.
- Tukey only applies to ANOVA, not to other cases of multiple testing.

Rats and vitamin B

- What is the effect of dietary vitamin B on the kidney?
- A number of rats were randomized to receive either a B-supplemented diet or a regular diet.
- Desired to control for initial size of rats, so classified into size classes lean and obese.
- After 20 weeks, rats' kidneys weighed.
- Variables:
 - Response: kidneyweight (grams).
 - Explanatory: diet, ratsize.
- Read in data:

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/vitaminb.txt"
vitaminb <- read_delim(my_url, " ")
```

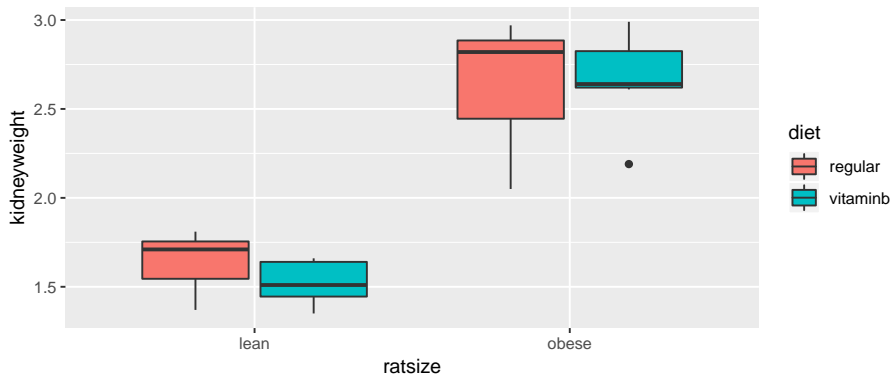

The data

```
vitaminb
```

```
## # A tibble: 28 x 3
##   ratsize diet      kidneyweight
##   <chr>   <chr>         <dbl>
## 1 lean    regular          1.62
## 2 lean    regular          1.8
## 3 lean    regular          1.71
## 4 lean    regular          1.81
## 5 lean    regular          1.47
## 6 lean    regular          1.37
## 7 lean    regular          1.71
## 8 lean    vitaminb         1.51
## 9 lean    vitaminb         1.65
## 10 lean   vitaminb         1.45
## # ... with 18 more rows
```

Grouped boxplot

```
ggplot(vitaminb, aes(  
  x = ratsize, y = kidneyweight,  
  fill = diet  
)) + geom_boxplot()
```



What's going on?

- Calculate group means:

```
summary <- vitaminb %>%
  group_by(ratsize, diet) %>%
  summarize(mean = mean(kidneyweight))
summary
```

```
## # A tibble: 4 x 3
## # Groups:   ratsize [2]
##   ratsize diet      mean
##   <chr>   <chr>   <dbl>
## 1 lean    regular    1.64
## 2 lean    vitaminb   1.53
## 3 obese   regular    2.64
## 4 obese   vitaminb   2.67
```

- Rat size: a large and consistent effect.
- Diet: small/no effect (compare same rat size, different diet).
- Effect of rat size *same* for each diet: no interaction.

ANOVA with interaction

```

vitaminb.1 <- aov(kidneyweight ~ ratsize * diet,
  data = vitaminb
)
summary(vitaminb.1)

```

```

##              Df Sum Sq Mean Sq F value    Pr(>F)
## ratsize         1   8.068    8.068 141.179 1.53e-11 ***
## diet            1   0.012    0.012   0.218   0.645
## ratsize:diet     1   0.036    0.036   0.638   0.432
## Residuals      24   1.372    0.057
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

- Significance/nonsignificance as we expected.
- Note no significant interaction (can be removed).

Interaction plot

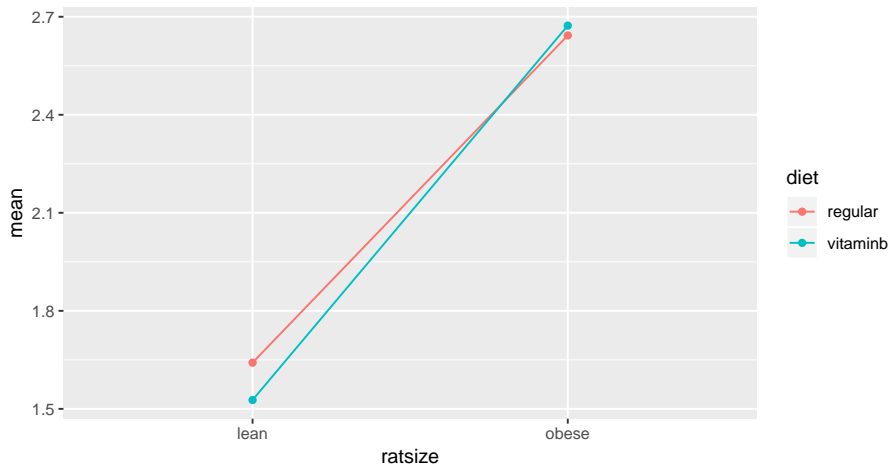
- Plot mean of response variable against one of the explanatory, using other one as groups. Start from summary:

```
g <- ggplot(summary, aes(  
  x = ratsize, y = mean,  
  colour = diet, group = diet  
)) +  
  geom_point() + geom_line()
```

- For this, have to give *both* group and colour.

The interaction plot

g



Take out interaction

```
vitaminb.2 <- update(vitaminb.1, . ~ . - ratsize:diet)
summary(vitaminb.2)
```

```
##              Df Sum Sq Mean Sq F value    Pr(>F)
## ratsize        1  8.068    8.068 143.256 7.59e-12 ***
## diet           1  0.012    0.012   0.221   0.643
## Residuals     25  1.408    0.056
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- No Tukey for diet: not significant.
- No Tukey for ratsize: only two sizes, and already know that obese rats have larger kidneys than lean ones.
- Bottom line: diet has no effect on kidney size once you control for size of rat.

The auto noise data

In 1973, the President of Texaco cited an automobile filter developed by Associated Octel Company as effective in reducing pollution. However, questions had been raised about the effects of filter silencing. He referred to the data included in the report (and below) as evidence that the silencing properties of the Octel filter were at least equal to those of standard silencers.

```
u <- "http://www.utsc.utoronto.ca/~butler/d29/autonoise.txt"
autonoise <- read_table(u)
```

```
## Parsed with column specification:
## cols(
##   noise = col_double(),
##   size = col_character(),
##   type = col_character(),
##   side = col_character()
## )
```


The data

```
autonoise
```

```
## # A tibble: 36 x 4
##   noise size type  side
##   <dbl> <chr> <chr> <chr>
## 1   840 M      Std    R
## 2   770 L      Octel  L
## 3   820 M      Octel  R
## 4   775 L      Octel  R
## 5   825 M      Octel  L
## 6   840 M      Std    R
## 7   845 M      Std    L
## 8   825 M      Octel  L
## 9   815 M      Octel  L
## 10  845 M      Std    R
## # ... with 26 more rows
```

Making boxplot

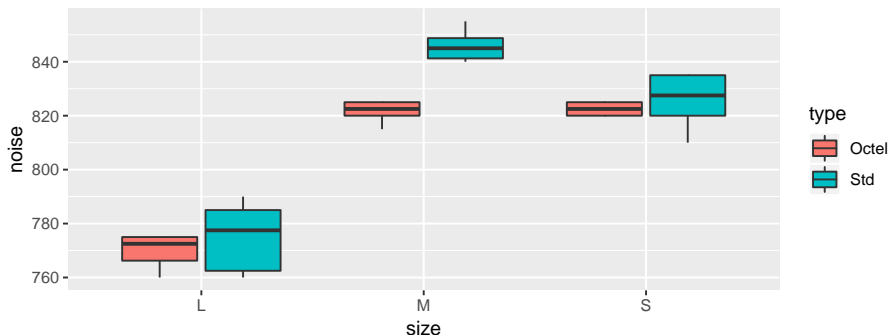
- Make a boxplot, but have combinations of filter type and engine size.
- Use grouped boxplot again, thus:

```
g <- autonoise %>%  
  ggplot(aes(x = size, y = noise, fill = type)) +  
  geom_boxplot()
```

The boxplot

- See difference in engine noise between Octel and standard is larger for medium engine size than for large or small.
- Some evidence of differences in spreads (ignore for now):

g



ANOVA

```
autonoise.1 <- aov(noise ~ size * type, data = autonoise)
summary(autonoise.1)
```

```
##              Df Sum Sq Mean Sq F value    Pr(>F)
## size          2  26051   13026  199.119 < 2e-16 ***
## type          1   1056    1056   16.146 0.000363 ***
## size:type      2    804     402    6.146 0.005792 **
## Residuals     30   1962      65
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- The interaction is significant, as we suspected from the boxplots.
- The within-group spreads don't look very equal, but only based on 6 obs each.

Tukey: ouch!

```
autonoise.2 <- TukeyHSD(autonoise.1)
autonoise.2$`size:type`
```

##		diff	lwr	upr	p adj
##	M:Octel-L:Octel	51.6666667	37.463511	65.869823	6.033496e-11
##	S:Octel-L:Octel	52.5000000	38.296844	66.703156	4.089762e-11
##	L:Std-L:Octel	5.0000000	-9.203156	19.203156	8.890358e-01
##	M:Std-L:Octel	75.8333333	61.630177	90.036489	4.962697e-14
##	S:Std-L:Octel	55.8333333	41.630177	70.036489	9.002910e-12
##	S:Octel-M:Octel	0.8333333	-13.369823	15.036489	9.999720e-01
##	L:Std-M:Octel	-46.6666667	-60.869823	-32.463511	6.766649e-10
##	M:Std-M:Octel	24.1666667	9.963511	38.369823	1.908995e-04
##	S:Std-M:Octel	4.1666667	-10.036489	18.369823	9.454142e-01
##	L:Std-S:Octel	-47.5000000	-61.703156	-33.296844	4.477636e-10
##	M:Std-S:Octel	23.3333333	9.130177	37.536489	3.129974e-04
##	S:Std-S:Octel	3.3333333	-10.869823	17.536489	9.787622e-01
##	M:Std-L:Std	70.8333333	56.630177	85.036489	6.583623e-14
##	S:Std-L:Std	50.8333333	36.630177	65.036489	8.937329e-11
##	S:Std-M:Std	-20.0000000	-34.203156	-5.796844	2.203265e-03

Interaction plot

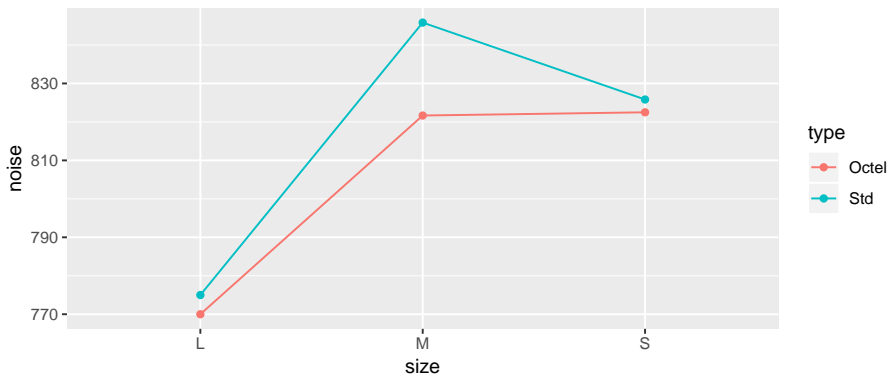
- This time, don't have summary of mean noise for each size-type combination.
- One way is to compute summaries (means) first, and feed into `ggplot` as in vitamin B example.
- Or, have `ggplot` compute them for us, thus:

```
g <- ggplot(autonoise, aes(  
  x = size, y = noise,  
  colour = type, group = type  
)) +  
  stat_summary(fun.y = mean, geom = "point") +  
  stat_summary(fun.y = mean, geom = "line")
```

Interaction plot

The lines are definitely *not* parallel, showing that the effect of type is different for medium-sized engines than for others:

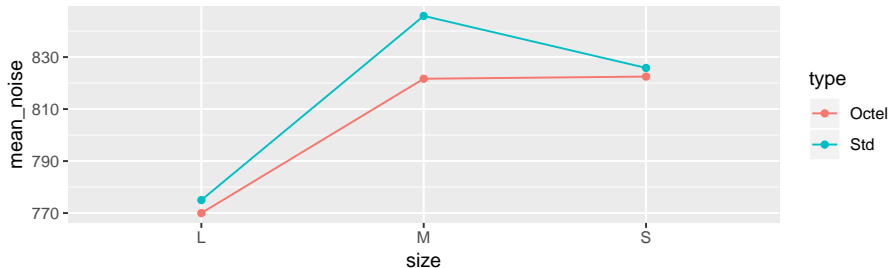
g



If you don't like that...

...then compute the means first, in a pipeline:

```
autonoise %>%
  group_by(size, type) %>%
  summarize(mean_noise = mean(noise)) %>%
  ggplot(aes(
    x = size, y = mean_noise, group = type,
    colour = type
  )) + geom_point() + geom_line()
```



Simple effects for auto noise example

- In auto noise example, weren't interested in all comparisons between car size and filter type combinations.
- Wanted to demonstrate (lack of) difference between filter types *for each car type*.
- These are called **simple effects** of one variable (filter type) conditional on other variable (car type).
- To do this, pull out just the data for small cars, compare noise for the two filter types. Then repeat for medium and large cars. (Three one-way ANOVAs.)

Do it using dplyr tools

- Small cars:

```
autonoise %>%
  filter(size == "S") %>%
  aov(noise ~ type, data = .) %>%
  summary()
```

```
##              Df Sum Sq Mean Sq F value Pr(>F)
## type          1   33.3   33.33    0.548  0.476
## Residuals    10  608.3   60.83
```

- No filter difference for small cars.
- For Medium, change S to M and repeat.

Simple effect of filter type for medium cars

```
{
autonoise %>%
  filter(size == "M") %>%
  aov(noise ~ type, data = .) %>%
  summary()

##              Df Sum Sq Mean Sq F value    Pr(>F)
## type           1 1752.1   1752.1    68.93 8.49e-06 ***
## Residuals     10   254.2     25.4
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

}
```

- There *is* an effect of filter type for medium cars. Look at means to investigate (over).

Mean noise for each filter type

...for medium engine size:

```
autonoise %>%
  filter(size == "M") %>%
  group_by(type) %>%
  summarize(m = mean(noise))
```

```
## # A tibble: 2 x 2
##   type      m
##   <chr> <dbl>
## 1 Octel  822.
## 2 Std    846.
```

- Octel filters produce *less* noise for medium cars.

Large cars

- Large cars:

```
autonoise %>%
  filter(size == "L") %>%
  aov(noise ~ type, data = .) %>%
  summary()
```

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
## type	1	75	75	0.682	0.428
## Residuals	10	1100	110		

- No significant difference again.

Or...

use glance from broom:

```
autonoise %>%
  filter(size == "L") %>%
  aov(noise ~ type, data = .) %>%
  glance()
```

```
## # A tibble: 1 x 11
##   r.squared adj.r.squared sigma statistic p.value    df
##   <dbl>      <dbl> <dbl>      <dbl>    <dbl> <int>
## 1    0.0638    -0.0298  10.5      0.682    0.428     2
## # ... with 5 more variables: logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, deviance <dbl>, df.residual <int>
```

- P-value same as from summary output.

All at once, using split/apply/combine

The “split” part:

```
autonoise %>%
  group_by(size) %>%
  nest()
```

```
## # A tibble: 3 x 2
##   size data
##   <chr> <list>
## 1 M     <tibble [12 x 3]>
## 2 L     <tibble [12 x 3]>
## 3 S     <tibble [12 x 3]>
```

Now have *three* rows, with the data frame for each size encoded as *one element* of this data frame.

Apply

- Write function to do aov on a data frame with columns noise and type, returning P-value:

```
aov_pval <- function(x) {
  noise.1 <- aov(noise ~ type, data = x)
  gg <- glance(noise.1)
  gg$p.value
}
```

- Test it:

```
autonoise %>%
  filter(size == "L") %>%
  aov_pval()
```

```
## [1] 0.428221
```

- Check.

Combine

- Apply this function to each of the nested data frames (one per engine size):

```
autonoise %>%
  group_by(size) %>%
  nest() %>%
  mutate(p_val = map_dbl(data, ~ aov_pval(.)))
```

```
## # A tibble: 3 x 3
##   size data                p_val
##   <chr> <list>                <dbl>
## 1 M    <tibble [12 x 3]> 0.00000849
## 2 L    <tibble [12 x 3]> 0.428
## 3 S    <tibble [12 x 3]> 0.476
```

- `map_dbl` because `aov_pval` returns a decimal number (a `dbl`). Investigate what happens if you use `map` instead.

Tidy up

- The data column was stepping-stone to getting answer. Don't need it any more:

```
simple_effects <- autonoise %>%
  group_by(size) %>%
  nest() %>%
  mutate(p_val = map_dbl(data, ~ aov_pval(.))) %>%
  select(-data)
simple_effects
```

```
## # A tibble: 3 x 2
##   size      p_val
##   <chr>    <dbl>
## 1 M      0.00000849
## 2 L      0.428
## 3 S      0.476
```

Simultaneous tests

- When testing simple effects, doing several tests at once. (In this case, 3.)
- Have to adjust P-values for this. Eg. Holm:

```
simple_effects %>%
  arrange(p_val) %>%
  mutate(multiplier = 4 - row_number()) %>%
  mutate(p_val_adj = p_val * multiplier)
```

```
## # A tibble: 3 x 4
##   size      p_val multiplier p_val_adj
##   <chr>    <dbl>      <dbl>    <dbl>
## 1 M      0.00000849          3 0.0000255
## 2 L      0.428              2 0.856
## 3 S      0.476              1 0.476
```

* No change in rejection decisions.

* Octel filters sig. better in terms of noise for medium cars, and not sig. different for other

Confidence intervals

- Perhaps better way of assessing simple effects: look at *confidence intervals* rather than tests.
- Gives us sense of accuracy of estimation, and thus whether non-significance might be lack of power: “absence of evidence is not evidence of absence”.
- Works here because *two* filter types, using *t*.test for each engine type.
- Want to show that the Octel filter is equivalent to or better than the standard filter, in terms of engine noise.

Equivalence and noninferiority

- Known as “equivalence testing” in medical world. A good read: [link](#). Basic idea: decide on size of difference δ that would be considered “equivalent”, and if CI entirely inside $\pm\delta$, have evidence in favour of equivalence.
- We really want to show that the Octel filters are “no worse” than the standard one: that is, equivalent *or better* than standard filters.
- Such a “noninferiority test” done by checking that upper limit of CI, new minus old, is *less* than δ . (This requires careful thinking about (i) which way around the difference is and (ii) whether a higher or lower value is better.)

CI for small cars

Same idea as for simple effect test:

```
autonoise %>%  
  filter(size == "S") %>%  
  t.test(noise ~ type, data = .) %>%  
  .[["conf.int"]]
```

```
## [1] -14.517462    7.850795  
## attr(,"conf.level")  
## [1] 0.95
```

CI for medium cars

```
autonoise %>%  
  filter(size == "M") %>%  
  t.test(noise ~ type, data = .) %>%  
  .[["conf.int"]]
```

```
## [1] -30.75784 -17.57549  
## attr(,"conf.level")  
## [1] 0.95
```

CI for large cars

```
autonoise %>%  
  filter(size == "L") %>%  
  t.test(noise ~ type, data = .) %>%  
  .[["conf.int"]]
```

```
## [1] -19.270673    9.270673  
## attr(,"conf.level")  
## [1] 0.95
```


Or, all at once: split/apply/combine

```
ci_func <- function(x) {  
  tt <- t.test(noise ~ type, data = x)  
  tt$conf.int  
}  
autonoise %>%  
  group_by(size) %>%  
  nest() %>%  
  mutate(ci = map(data, ~ ci_func(.))) %>%  
  unnest(ci) -> cis
```

Results

```
cis
```

```
## # A tibble: 6 x 2
##   size      ci
##   <chr>  <dbl>
## 1 M     -30.8
## 2 M     -17.6
## 3 L     -19.3
## 4 L       9.27
## 5 S     -14.5
## 6 S       7.85
```

Procedure

- Function to get CI of difference in noise means for types of filter on input data frame
- Group by size, nest (mini-df per size)
- Calculate CI for each thing in data (ie. each size). `map`: CI is two numbers long
- `unnest ci` column to see two numbers in each CI.

CIs and noninferiority test

- Suppose we decide that a 20 dB difference would be considered equivalent. (I have no idea whether that is reasonable.)
- Intervals:

```
cis %>%
  mutate(hilo = rep(c("lower", "upper"), 3)) %>%
  spread(hilo, ci)
```

```
## # A tibble: 3 x 3
##   size lower upper
##   <chr> <dbl> <dbl>
## 1 L     -19.3   9.27
## 2 M     -30.8  -17.6
## 3 S     -14.5   7.85
```

Comments

- In all cases, upper limit of CI is less than 20 dB. The Octel filters are “noninferior” to the standard ones.
- Caution: we did 3 procedures at once again. The true confidence level is not 95%. (Won't worry about that here.)

Contrasts in ANOVA

- Sometimes, don't want to compare *all* groups, only *some* of them.
- Might be able to specify these comparisons ahead of time; other comparisons of no interest.
- Wasteful to do ANOVA and Tukey.

Example: chainsaw kickback

- From link.
- Forest manager concerned about safety of chainsaws issued to field crew. 4 models of chainsaws, measure “kickback” (degrees of deflection) for 5 of each:

A	B	C	D

42	28	57	29
17	50	45	29
24	44	48	22
39	32	41	34
43	61	54	30

- So far, standard 1-way ANOVA: what differences are there among models?

chainsaw kickback (2)

- But: models A and D are designed to be used at home, while models B and C are industrial models.
- Suggests these comparisons of interest:
- home vs. industrial
- the two home models A vs. D
- the two industrial models B vs. C.
- Don't need to compare *all* the pairs of models.

What is a contrast?

- Contrast is a linear combination of group means.
- Notation: μ_A for (population) mean of group A , and so on.
- In example, compare two home models: $H_0 : \mu_A - \mu_D = 0$.
- Compare two industrial models: $H_0 : \mu_B - \mu_C = 0$.
- Compare average of two home models vs. average of two industrial models: $H_0 : \frac{1}{2}(\mu_A + \mu_D) - \frac{1}{2}(\mu_B + \mu_C) = 0$ or $H_0 : 0.5\mu_A - 0.5\mu_B - 0.5\mu_C + 0.5\mu_D = 0$.
- Note that coefficients of contrasts add to 0, and right-hand side is 0.

Contrasts in R

- Comparing two home models A and D ($\mu_A - \mu_D = 0$):

```
c.home <- c(1, 0, 0, -1)
```

- Comparing two industrial models B and C ($\mu_B - \mu_C = 0$):

```
c.industrial <- c(0, 1, -1, 0)
```

- Comparing home average vs. industrial average
($0.5\mu_A - 0.5\mu_B - 0.5\mu_C + 0.5\mu_D = 0$):

```
c.home.ind <- c(0.5, -0.5, -0.5, 0.5)
```

Orthogonal contrasts

- What happens if we multiply the contrast coefficients one by one?

```
c.home * c.industrial
```

```
## [1] 0 0 0 0
```

```
c.home * c.home.ind
```

```
## [1] 0.5 0.0 0.0 -0.5
```

```
c.industrial * c.home.ind
```

```
## [1] 0.0 -0.5 0.5 0.0
```

- in each case, the results **add up to zero**. Such contrasts are called **orthogonal**.

Orthogonal contrasts (2)

- Compare these:

```
c1 <- c(1, -1, 0)
c2 <- c(0, 1, -1)
sum(c1 * c2)
```

```
## [1] -1
```

Not zero, so $c1$ and $c2$ are *not* orthogonal.

- Orthogonal contrasts are much easier to deal with.
- Can use non-orthogonal contrasts, but more trouble (beyond us).

Read in data

```
url <- "http://www.utsc.utoronto.ca/~butler/d29/chainsaw.txt"
chain.wide <- read_table(url)
chain.wide
```

```
## # A tibble: 5 x 4
##       A      B      C      D
##   <dbl> <dbl> <dbl> <dbl>
## 1    42    28    57    29
## 2    17    50    45    29
## 3    24    44    48    22
## 4    39    32    41    34
## 5    43    61    54    30
```

Tidying

Need all the kickbacks in *one* column:

```
chain <- gather(chain.wide, model, kickback, A:D,  
  factor_key = T  
)
```

Starting the analysis (2)

The proper data frame (tiny):

```
chain
```

```
## # A tibble: 20 x 2
##   model kickback
##   <fct>      <dbl>
## 1 A          42
## 2 A          17
## 3 A          24
## 4 A          39
## 5 A          43
## 6 B          28
## 7 B          50
## 8 B          44
## 9 B          32
## 10 B         61
## 11 C          57
## 12 C          45
## 13 C          48
## 14 C          41
## 15 C          54
## 16 D          29
## 17 D          29
## 18 D          22
## 19 D          34
## 20 D          30
```

Setting up contrasts

```
m <- cbind(c.home, c.industrial, c.home.ind)
m
```

```
##      c.home c.industrial c.home.ind
## [1,]      1           0         0.5
## [2,]      0           1        -0.5
## [3,]      0          -1        -0.5
## [4,]     -1           0         0.5
```

```
contrasts(chain$model) <- m
```


ANOVA as if regression

```
chain.1 <- lm(kickback ~ model, data = chain)
summary(chain.1)
```

```
##
## Call:
## lm(formula = kickback ~ model, data = chain)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -16.00  -7.10   0.60   6.25  18.00
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      38.450      2.179  17.649 6.52e-12 ***
## modelc.home        2.100      3.081   0.682 0.50524
## modelc.industrial  -3.000      3.081  -0.974 0.34469
## modelc.home.ind    -15.100     4.357  -3.466 0.00319 **
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.743 on 16 degrees of freedom
## Multiple R-squared:  0.4562, Adjusted R-squared:  0.3542
## F-statistic: 4.474 on 3 and 16 DF, p-value: 0.01822
```

Conclusions

```
tidy(chain.1) %>% select(term, p.value)
```

```
## # A tibble: 4 x 2
##   term                p.value
##   <chr>              <dbl>
## 1 (Intercept)        6.52e-12
## 2 modelc.home         5.05e- 1
## 3 modelc.industrial  3.45e- 1
## 4 modelc.home.ind     3.19e- 3
```

- Two home models not sig. diff. (P-value 0.51)
- Two industrial models not sig. diff. (P-value 0.34)
- Home, industrial models *are* sig. diff. (P-value 0.0032).

Means by model

- The means:

```
chain %>%
  group_by(model) %>%
  summarize(mean.kick = mean(kickback)) %>%
  arrange(desc(mean.kick))
```

```
## # A tibble: 4 x 2
##   model mean.kick
##   <fct>     <dbl>
## 1 C         49
## 2 B         43
## 3 A         33
## 4 D        28.8
```

- Home models A & D have less kickback than industrial ones B & C.
- Makes sense because industrial users should get training to cope with additional kickback.

Section 6

Analysis of covariance

Analysis of covariance

- ANOVA: explanatory variables categorical (divide data into groups)
- traditionally, analysis of covariance has categorical x 's plus one numerical x ("covariate") to be adjusted for.
- `lm` handles this too.
- Simple example: two treatments (drugs) (a and b), with before and after scores.
- Does knowing before score and/or treatment help to predict after score?
- Is after score different by treatment/before score?

Data

Treatment, before, after:

a 5 20
a 10 23
a 12 30
a 9 25
a 23 34
a 21 40
a 14 27
a 18 38
a 6 24
a 13 31
b 7 19
b 12 26
b 27 33
b 24 35
b 18 30
b 22 31
b 26 34
b 21 28
b 14 23
b 9 22

Packages

tidyverse and broom:

```
library(tidyverse)  
library(broom)
```

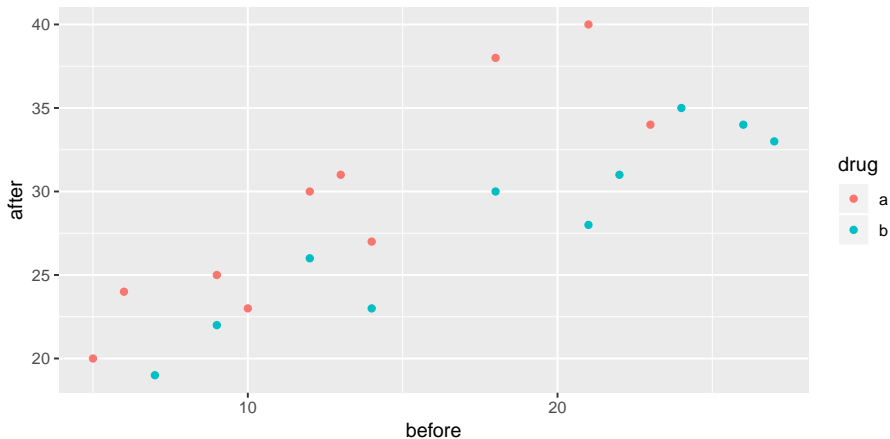
Read in data

```
url <- "http://www.utsc.utoronto.ca/~butler/d29/ancova.txt"
prepost <- read_delim(url, " ")
prepost %>% sample_n(9) # randomly chosen rows
```

```
## # A tibble: 9 x 3
##   drug   before after
##   <chr>   <dbl> <dbl>
## 1 a         13     31
## 2 a          9     25
## 3 a         18     38
## 4 b         12     26
## 5 b         27     33
## 6 a         14     27
## 7 a         10     23
## 8 b          9     22
## 9 a          5     20
```


Making a plot

```
ggplot(prepost, aes(x = before, y = after, colour = drug)) +  
  geom_point()
```



Comments

- As before score goes up, after score goes up.
- Red points (drug A) generally above blue points (drug B), for comparable before score.
- Suggests before score effect *and* drug effect.

The means

```
prepost %>%
  group_by(drug) %>%
  summarize(
    before_mean = mean(before),
    after_mean = mean(after)
  )
```

```
## # A tibble: 2 x 3
##   drug   before_mean after_mean
##   <chr>         <dbl>         <dbl>
## 1 a             13.1             29.2
## 2 b             18              28.1
```

- Mean “after” score slightly higher for treatment A.
- Mean “before” score much higher for treatment B.
- Greater *improvement* on treatment A.

Testing for interaction

```
prepost.1 <- lm(after ~ before * drug, data = prepost)
anova(prepost.1)
```

```
## Analysis of Variance Table
```

```
##
```

```
## Response: after
```

```
##           Df Sum Sq Mean Sq F value    Pr(>F)
## before      1  430.92   430.92  62.6894  6.34e-07 ***
## drug        1  115.31   115.31  16.7743  0.0008442 ***
## before:drug  1   12.34    12.34   1.7948  0.1990662
## Residuals   16  109.98     6.87
```

```
## ---
```

```
## Signif. codes:
```

```
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Interaction not significant. Will remove later.

Predictions, with interaction included

Make combinations of before score and drug:

```
new <- crossing(
  before = c(5, 15, 25),
  drug = c("a", "b")
)
new
```

```
## # A tibble: 6 x 2
##   before drug
##   <dbl> <chr>
## 1      5 a
## 2      5 b
## 3     15 a
## 4     15 b
## 5     25 a
## 6     25 b
```

Do predictions:

```
pred <- predict(prepost.1, new)
preds <- bind_cols(new, pred = pred)
preds
```

```
## # A tibble: 6 x 3
##   before drug    pred
##   <dbl> <chr> <dbl>
## 1      5 a      21.3
## 2      5 b      18.7
## 3     15 a      31.1
## 4     15 b      25.9
## 5     25 a      40.8
## 6     25 b      33.2
```

Making a plot with lines for each drug

```
g <- ggplot(prepost,
  aes(x = before, y = after, colour = drug)) +
  geom_point() + geom_line(data = preds, aes(y = pred))
```

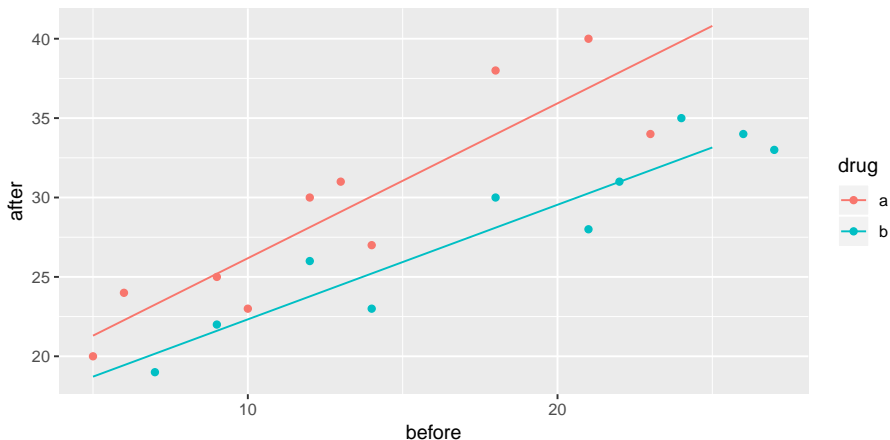
- Here, final line:
 - joins points by lines *for different data set* (preds rather than prepost),
 - *different y* (pred rather than after),
 - but same *x* (x=before inherited from first aes).
- Last line could (more easily) be

```
geom_smooth(method = "lm", se = F)
```

which would work here, but not for later plot.

The plot

- Lines almost parallel, but not quite.
- Non-parallelism (interaction) not significant:



Taking out interaction

```
prepost.2 <- update(prepost.1, . ~ . - before:drug)
anova(prepost.2)
```

```
## Analysis of Variance Table
##
## Response: after
##           Df Sum Sq Mean Sq F value    Pr(>F)
## before      1 430.92   430.92   59.890 5.718e-07 ***
## drug        1  115.31    115.31   16.025 0.0009209 ***
## Residuals  17  122.32      7.20
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Take out non-significant interaction.
- before and drug strongly significant.
- Do predictions again and plot them.

Predicted values again (no-interaction model)

```
pred <- predict(prepost.2, new)
preds <- bind_cols(new, pred = pred)
preds
```

```
## # A tibble: 6 x 3
##   before drug    pred
##   <dbl> <chr> <dbl>
## 1      5 a      22.5
## 2      5 b      17.3
## 3     15 a      30.8
## 4     15 b      25.6
## 5     25 a      39.0
## 6     25 b      33.9
```

Each increase of 10 in before score results in 8.3 in predicted after score, *the same for both drugs*.

Making a plot, again

```
g <- ggplot(  
  prepost,  
  aes(x = before, y = after, colour = drug)  
) +  
  geom_point() +  
  geom_line(data = preds, aes(y = pred))
```

Exactly same as before, but using new predictions.

The no-interaction plot of predicted values

g

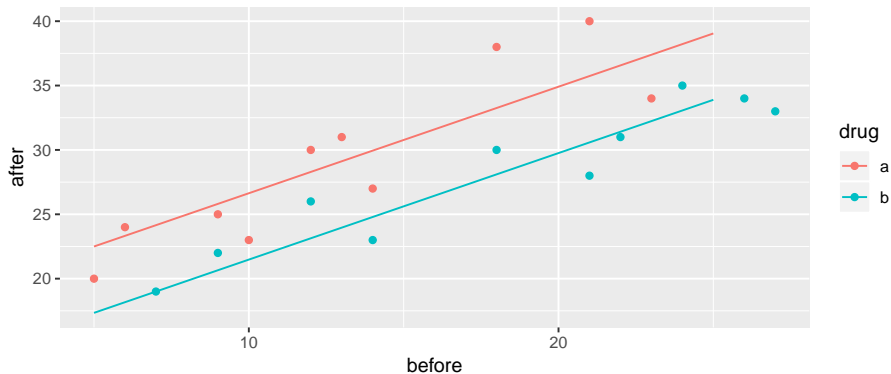


Figure 40: plot of chunk cabazzo

Different look at model output

- `anova(prepost.2)` tests for significant effect of before score and of drug, but doesn't help with interpretation.
- `summary(prepost.2)` views as regression with slopes:

```
summary(prepost.2)
```

```
##
## Call:
## lm(formula = after ~ before + drug, data = prepost)
##
## Residuals:
```

	Min	1Q	Median	3Q	Max
	-3.6348	-2.5099	-0.2038	1.8871	4.7453

```
##
## Coefficients:
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	18.3600	1.5115	12.147	8.35e-10 ***
before	0.8275	0.0955	8.665	1.21e-07 ***
drugb	-5.1547	1.2876	-4.003	0.000921 ***

```
## ---
## Signif. codes:
```

	0	***	0.001	**	0.01	*	0.05	.	0.1		1

Understanding those slopes

```
tidy(prepost.2)
```

```
## # A tibble: 3 x 5
##   term          estimate std.error statistic  p.value
##   <chr>         <dbl>     <dbl>     <dbl>   <dbl>
## 1 (Intercept)    18.4       1.51      12.1  8.35e-10
## 2 before         0.827     0.0955     8.66  1.21e- 7
## 3 drugb        -5.15      1.29     -4.00  9.21e- 4
```

- before ordinary numerical variable; drug categorical.
- lm uses first category *druga* as baseline.
- Intercept is prediction of after score for before score 0 and *drug A*.
- before slope is predicted change in after score when before score increases by 1 (usual slope)
- Slope for drugb is *change* in predicted after score for being on drug B rather than drug A. Same for *any* before score (no interaction).

Summary

- ANCOVA model: fits different regression line for each group, predicting response from covariate.
- ANCOVA model with interaction between factor and covariate allows different slopes for each line.
- Sometimes those lines can cross over!
- If interaction not significant, take out. Lines then parallel.
- With parallel lines, groups have consistent effect regardless of value of covariate.

Section 7

Multivariate ANOVA

Multivariate analysis of variance

- Standard ANOVA has just one response variable.
- What if you have more than one response?
- Try an ANOVA on each response separately.
- But might miss some kinds of interesting dependence between the responses that distinguish the groups.

Packages

```
library(car)  
library(tidyverse)
```

Small example

- Measure yield and seed weight of plants grown under 2 conditions: low and high amounts of fertilizer.
- Data (fertilizer, yield, seed weight):

```
url <- "http://www.utsc.utoronto.ca/~butler/d29/manova1.txt"  
hilo <- read_delim(url, " ")
```

```
## Parsed with column specification:  
## cols(  
##   fertilizer = col_character(),  
##   yield = col_double(),  
##   weight = col_double()  
## )
```

- 2 responses, yield and seed weight.

The data

```
hilo
```

```
## # A tibble: 8 x 3
##   fertilizer yield weight
##   <chr>      <dbl>  <dbl>
## 1 low        34      10
## 2 low        29      14
## 3 low        35      11
## 4 low        32      13
## 5 high       33      14
## 6 high       38      12
## 7 high       34      13
## 8 high       35      14
```

Boxplot for yield for each fertilizer group

```
ggplot(hilo, aes(x = fertilizer, y = yield)) + geom_boxplot()
```

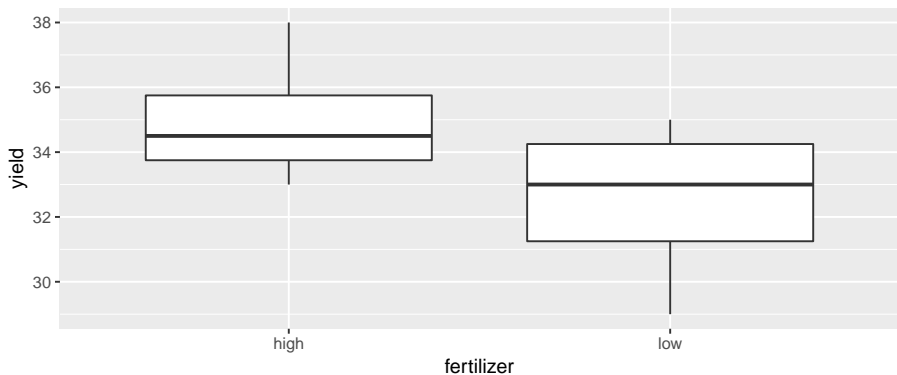


Figure 41: plot of chunk ferto

Boxplot for weight for each fertilizer group

```
ggplot(hilo, aes(x = fertilizer, y = weight)) + geom_boxplot()
```

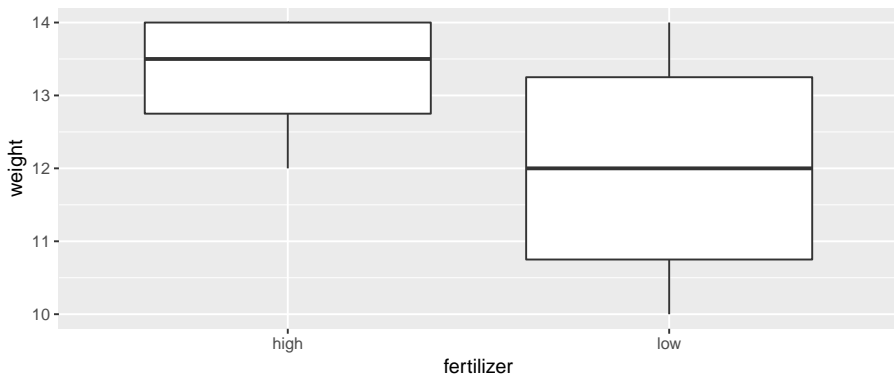


Figure 42: plot of chunk casteldisangro

ANOVAs for yield and weight

```
hilo.y <- aov(yield ~ fertilizer, data = hilo)
summary(hilo.y)
```

```
##                Df Sum Sq Mean Sq F value Pr(>F)
## fertilizer      1   12.5   12.500    2.143   0.194
## Residuals       6   35.0    5.833
```

```
hilo.w <- aov(weight ~ fertilizer, data = hilo)
summary(hilo.w)
```

```
##                Df Sum Sq Mean Sq F value Pr(>F)
## fertilizer      1   3.125    3.125    1.471   0.271
## Residuals       6  12.750    2.125
```

Neither response depends significantly on fertilizer. But...

Plotting both responses at once

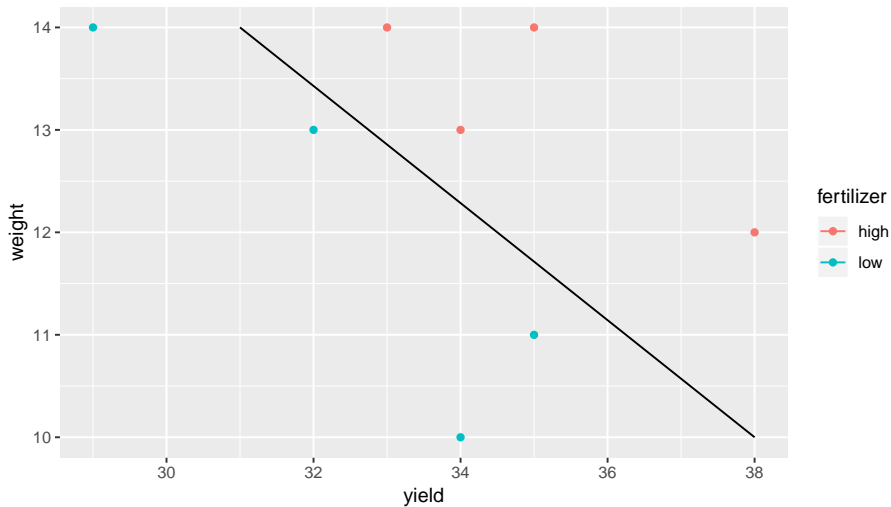
- Have two response variables (not more), so can plot the response variables against *each other*, labelling points by which fertilizer group they're from.
- First, create data frame with points (31, 14) and (38, 10) (why? Later):

```
d <- tribble(
  ~line_x, ~line_y,
  31, 14,
  38, 10
)
```

- Then plot data as points, and add line through points in d:

```
g <- ggplot(hilo, aes(x = yield, y = weight,
                      colour = fertilizer)) + geom_point() +
  geom_line(data = d,
            aes(x = line_x, y = line_y, colour = NULL))
```


The plot



Comments

- Graph construction:
 - Joining points in `d` by line.
 - `geom_line` inherits `colour` from `aes` in `ggplot`.
 - Data frame `d` has no `fertilizer` (previous `colour`), so have to unset.
- Results:
 - High-fertilizer plants have both yield and weight high.
 - True even though no sig difference in yield or weight individually.
 - Drew line separating highs from lows on plot.

MANOVA finds multivariate differences

- Is difference found by diagonal line significant? MANOVA finds out.

```
response <- with(hilo, cbind(yield, weight))
hilo.1 <- manova(response ~ fertilizer, data = hilo)
summary(hilo.1)
```

```
##              Df  Pillai approx F num Df den Df  Pr(>F)
## fertilizer    1 0.80154    10.097      2      5 0.01755 *
## Residuals     6
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Yes! Difference between groups is *diagonally*, not just up/down (weight) or left-right (yield). The *yield-weight combination* matters.

Strategy

- Create new response variable by gluing together columns of responses, using `cbind`.
- Use `manova` with new response, looks like `lm` otherwise.
- With more than 2 responses, cannot draw graph. What then?
- If MANOVA test significant, cannot use Tukey. What then?
- Use *discriminant analysis* (of which more later).

Another way to do MANOVA

Install (once) and load package car:

```
library(car)
```

Another way...

```
hilo.2.lm <- lm(response ~ fertilizer, data = hilo)
hilo.2 <- Manova(hilo.2.lm)
hilo.2
```

```
##
## Type II MANOVA Tests: Pillai test statistic
##              Df test stat approx F num Df den Df  Pr(>F)
## fertilizer   1    0.80154    10.097      2      5 0.01755 *
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Same result as small-m manova.
- Manova will also do *repeated measures*, coming up later.

Another example: peanuts

- Three different varieties of peanuts (mysteriously, 5, 6 and 8) planted in two different locations.
- Three response variables: *y*, *smk* and *w*.

```
u <- "http://www.utsc.utoronto.ca/~butler/d29/peanuts.txt"
peanuts.orig <- read_delim(u, " ")
```

```
## Parsed with column specification:
```

```
## cols(
```

```
##   obs = col_double(),
```

```
##   location = col_double(),
```

```
##   variety = col_double(),
```

```
##   y = col_double(),
```

```
##   smk = col_double(),
```

```
##   w = col_double()
```

```
## )
```

The data

```
peanuts.orig
```

```
## # A tibble: 12 x 6
```

```
##      obs location variety      y      smk      w
##      <dbl>      <dbl>    <dbl> <dbl> <dbl> <dbl>
##  1      1          1        5  195.  153.  51.4
##  2      2          1        5  194.  168.  53.7
##  3      3          2        5  190.  140.  55.5
##  4      4          2        5  180.  121.  44.4
##  5      5          1        6  203.  157.  49.8
##  6      6          1        6  196.  166.  45.8
##  7      7          2        6  203.  166.  60.4
##  8      8          2        6  198.  162.  54.1
##  9      9          1        8  194.  164.  57.8
## 10     10          1        8  187.  165.  58.6
## 11     11          2        8  202.  167.   65
## 12     12          2        8  200.  174.  67.2
```


Setup for analysis

```
peanuts <- peanuts.orig %>%  
  mutate(  
    location = factor(location),  
    variety = factor(variety)  
  )  
response <- with(peanuts, cbind(y, smk, w))  
head(response)
```

```
##           y    smk    w  
## [1,] 195.3 153.1 51.4  
## [2,] 194.3 167.7 53.7  
## [3,] 189.7 139.5 55.5  
## [4,] 180.4 121.1 44.4  
## [5,] 203.0 156.8 49.8  
## [6,] 195.9 166.0 45.8
```

Analysis (using Manova)

```
peanuts.1 <- lm(response ~ location * variety, data = peanuts)
peanuts.2 <- Manova(peanuts.1)
peanuts.2
```

```
##
## Type II MANOVA Tests: Pillai test statistic
##
```

	Df	test stat	approx F	num Df	den Df
location	1	0.89348	11.1843	3	4
variety	2	1.70911	9.7924	6	10
location:variety	2	1.29086	3.0339	6	10

```
##
```

	Pr(>F)
location	0.020502 *
variety	0.001056 **
location:variety	0.058708 .

```
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Comments

- Interaction not quite significant, but main effects are.
- Combined response variable (y, \mathbf{smk}, w) definitely depends on location and on variety
- Weak dependence of (y, \mathbf{smk}, w) on the location-variety *combination*.
- Understanding that dependence beyond our scope right now.

Section 8

Repeated measures by profile analysis

Repeated measures by profile analysis

- More than one response *measurement* for each subject. Might be
- measurements of the same thing at different times
- measurements of different but related things
- Generalization of matched pairs (“matched triples”, etc.).
- Variation: each subject does several different treatments at different times (called *crossover design*).
- Expect measurements on same subject to be correlated, so assumptions of independence will fail.
- Called *repeated measures*. Different approaches, but *profile analysis* uses Manova (set up right way).
- Another approach uses *mixed models* (random effects).

Packages

```
library(car)  
library(tidyverse)
```

Example: histamine in dogs

- 8 dogs take part in experiment.
- Dogs randomized to one of 2 different drugs.
- Response: log of blood concentration of histamine 0, 1, 3 and 5 minutes after taking drug. (Repeated measures.)
- Data in `dogs.txt`, column-aligned.

Read in data

```
my_url <- "http://www.utsc.utoronto.ca/~butler/d29/dogs.txt"
dogs <- read_table(my_url)
```

```
## Parsed with column specification:
## cols(
##   dog = col_character(),
##   drug = col_character(),
##   x = col_character(),
##   lh0 = col_double(),
##   lh1 = col_double(),
##   lh3 = col_double(),
##   lh5 = col_double()
## )
```


Setting things up

```
dogs
```

```
## # A tibble: 8 x 7
```

```
##   dog   drug      x      lh0    lh1    lh3    lh5
##   <chr> <chr>    <chr> <dbl> <dbl> <dbl> <dbl>
## 1 A     Morphine N     -3.22 -1.61 -2.3  -2.53
## 2 B     Morphine N     -3.91 -2.81 -3.91 -3.91
## 3 C     Morphine N     -2.66  0.34 -0.73 -1.43
## 4 D     Morphine N     -1.77 -0.56 -1.05 -1.43
## 5 E     Trimethaphan N    -3.51 -0.48 -1.17 -1.51
## 6 F     Trimethaphan N    -3.51  0.05 -0.31 -0.51
## 7 G     Trimethaphan N    -2.66 -0.19  0.07 -0.22
## 8 H     Trimethaphan N    -2.41  1.14  0.72  0.21
```

```
response <- with(dogs, cbind(lh0, lh1, lh3, lh5))
dogs.1 <- lm(response ~ drug, data = dogs)
```

The repeated measures MANOVA

Get list of response variable names; we call them times. Save in data frame.

```
times <- colnames(response)
times.df <- data.frame(times)
dogs.2 <- Manova(dogs.1,
  idata = times.df,
  idesign = ~times
)
dogs.2
```

```
##
## Type II Repeated Measures MANOVA Tests: Pillai test statistic
##
```

	Df	test	stat	approx	F	num	Df	den	Df	Pr(>F)
## (Intercept)	1	0.76347	19.3664	1	6	0.004565	**			
## drug	1	0.34263	3.1272	1	6	0.127406				
## times	1	0.94988	25.2690	3	4	0.004631	**			
## drug:times	1	0.89476	11.3362	3	4	0.020023	*			

```
## ---
## Signif. codes:
```

Wide and long format

- Interaction significant. Pattern of response over time different for the two drugs.
- Want to investigate interaction.

The wrong shape

- But data frame has several observations per line (“wide format”):

```
dogs %>% slice(1:6)
```

```
## # A tibble: 6 x 7
##   dog   drug      x      lh0    lh1    lh3    lh5
##   <chr> <chr>    <chr> <dbl> <dbl> <dbl> <dbl>
## 1 A     Morphine  N     -3.22 -1.61 -2.3  -2.53
## 2 B     Morphine  N     -3.91 -2.81 -3.91 -3.91
## 3 C     Morphine  N     -2.66  0.34 -0.73 -1.43
## 4 D     Morphine  N     -1.77 -0.56 -1.05 -1.43
## 5 E     Trimethaphan N     -3.51 -0.48 -1.17 -1.51
## 6 F     Trimethaphan N     -3.51  0.05 -0.31 -0.51
```

- Plotting works with data in “long format”: one response per line.
- The responses are log-histamine at different times, labelled lh-something. Call them all lh and put them in one column, with the time they belong to labelled.

Running gather, try 1

```
dogs %>% gather(time, lh, lh0:lh5)
```

```
## # A tibble: 32 x 5
```

```
##   dog   drug      x    time    lh
##   <chr> <chr>    <chr> <chr> <dbl>
## 1 A     Morphine  N     lh0   -3.22
## 2 B     Morphine  N     lh0   -3.91
## 3 C     Morphine  N     lh0   -2.66
## 4 D     Morphine  N     lh0   -1.77
## 5 E     Trimethaphan N     lh0   -3.51
## 6 F     Trimethaphan N     lh0   -3.51
## 7 G     Trimethaphan N     lh0   -2.66
## 8 H     Trimethaphan N     lh0   -2.41
## 9 A     Morphine  N     lh1   -1.61
## 10 B    Morphine  N     lh1   -2.81
## # ... with 22 more rows
```

Getting the times

Not quite right: for the times, we want just the numbers, not the letters lh every time. Want new variable containing just number in time:

parse_number.

```
dogs %>%
  gather(timex, lh, lh0:lh5) %>%
  mutate(time = parse_number(timex))
```

```
## # A tibble: 32 x 6
```

##	dog	drug	x	timex	lh	time
##	<chr>	<chr>	<chr>	<chr>	<dbl>	<dbl>
## 1	A	Morphine	N	lh0	-3.22	0
## 2	B	Morphine	N	lh0	-3.91	0
## 3	C	Morphine	N	lh0	-2.66	0
## 4	D	Morphine	N	lh0	-1.77	0
## 5	E	Trimethaphan	N	lh0	-3.51	0
## 6	F	Trimethaphan	N	lh0	-3.51	0
## 7	G	Trimethaphan	N	lh0	-2.66	0
## 8	H	Trimethaphan	N	lh0	-2.41	0
## 9	A	Morphine	N	lh1	-1.61	1

What I did differently

- I realized that `gather` was going to produce something like `lh1`, which I needed to do something further with, so this time I gave it a temporary name `timex`.
- This enabled me to use the name `time` for the actual numeric time.
- This works now, so next save into a new data frame `dogs.long`.

Saving the pipelined results

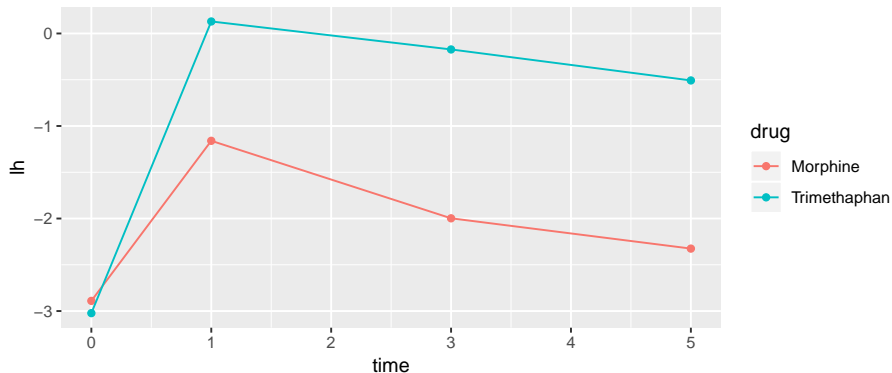
```
dogs %>%  
  gather(timex, lh, lh0:lh5) %>%  
  mutate(time = parse_number(timex)) -> dogs.long
```

This says:

- Take data frame `dogs`, and then:
- Combine the columns `lh0` through `lh5` into one column called `lh`, with the column that each `lh` value originally came from labelled by `timex`, and then:
- Pull out numeric values in `timex`, saving in `time` and then:
- save the result in a data frame `dogs.long`.

Interaction plot

```
ggplot(dogs.long, aes(x = time, y = lh,
                      colour = drug, group = drug)) +
  stat_summary(fun.y = mean, geom = "point") +
  stat_summary(fun.y = mean, geom = "line")
```



Comments

- Plot mean 1h value at each time, joining points on same drug by lines.
- drugs same at time 0
- after that, Trimethaphan higher than Morphine.
- Effect of drug not consistent over time: significant interaction.

Take out time zero

- Lines on interaction plot would then be parallel, and so interaction should no longer be significant.
- Go back to original “wide” dogs data frame.

```
response <- with(dogs, cbind(lh1, lh3, lh5)) # excl time 0
dogs.1 <- lm(response ~ drug, data = dogs)
times <- colnames(response)
times.df <- data.frame(times)
dogs.2 <- Manova(dogs.1,
  idata = times.df,
  idesign = ~times
)
```

Results and comments

dogs.2

```
##
## Type II Repeated Measures MANOVA Tests: Pillai test statistic
##              Df test stat approx F num Df den Df    Pr(>F)
## (Intercept)  1    0.54582    7.2106      1      6 0.036281 *
## drug         1    0.44551    4.8207      1      6 0.070527 .
## times        1    0.85429   14.6569      2      5 0.008105 **
## drug:times    1    0.43553    1.9289      2      5 0.239390
## ---
## Signif. codes:
## 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Correct: interaction no longer significant.
- Significant effect of time.
- Drug effect not quite significant (some variety among dogs within drug).

Is the non-significant drug effect reasonable?

- Plot *actual data*: lh against days, labelling observations by drug: “spaghetti plot”.
- Uses long data frame (confusing, yes I know):
- Plot (time, lh) points coloured by drug
- and connecting measurements for each *dog* by lines.
- This time, we want group=dog (want the measurements for each *dog* joined by lines), but colour=drug:

```
g <- ggplot(dogs.long, aes(
  x = time, y = lh,
  colour = drug, group = dog
)) +
  geom_point() + geom_line()
```

The graph displays the natural logarithm of the inhibitory current ($\ln(I_h)$) over time (0 to 5 minutes) for two drugs: Morphine (red lines) and Trimethaphan (teal lines). Morphine shows a peak at time 1 followed by a decline. Trimethaphan shows a peak at time 1 followed by a decline, with one line remaining high.

Time (min)	Morphine 1	Morphine 2	Morphine 3	Morphine 4	Morphine 5	Trimethaphan 1	Trimethaphan 2	Trimethaphan 3	Trimethaphan 4	Trimethaphan 5
0	-3.2	-3.8	-3.9	-2.8	-3.9	-2.4	-2.6	-2.6	-2.6	-2.6
1	0.3	-1.6	-2.8	-0.5	-1.6	1.1	0.0	-0.2	-0.5	-0.5
3	-0.7	-1.0	-2.3	-1.1	-2.3	0.7	0.1	-0.3	-1.1	-1.1
5	-1.4	-1.4	-2.5	-1.4	-2.5	0.2	-0.2	-0.5	-1.4	-1.4

Comments

- For each dog over time, there is a strong increase and gradual decrease in log-histamine. This explains the significant time effect.
- The pattern is more or less the same for each dog, regardless of drug. This explains the non-significant interaction.
- Most of the trimethaphan dogs (blue) have higher log-histamine throughout (time 1 and after), and some of the morphine dogs have lower.
- *But* two of the morphine dogs have log-histamine profiles like the trimethaphan dogs. This ambiguity is probably why the drug effect is not quite significant.

The exercise data

- 30 people took part in an exercise study.
- Each subject was randomly assigned to one of two diets (“low fat” or “non-low fat”) and to one of three exercise programs (“at rest”, “walking”, “running”).
- There are $2 \times 3 = 6$ experimental treatments, and thus each one is replicated $30/6 = 5$ times.
- Nothing unusual so far.
- However, each subject had their pulse rate measured at three different times (1, 15 and 30 minutes after starting their exercise), so have repeated measures.

Reading the data

Separated by *tabs*:

```
url <- "http://www.utsc.utoronto.ca/~butler/d29/exercise.txt"
exercise.long <- read_tsv(url)
```

```
## Parsed with column specification:
## cols(
##   id = col_double(),
##   diet = col_character(),
##   exerttype = col_character(),
##   pulse = col_double(),
##   time = col_character()
## )
```

The data

```
exercise.long %>% slice(1:8)
```

```
## # A tibble: 8 x 5
##       id diet      exertype pulse time
##   <dbl> <chr>      <chr>    <dbl> <chr>
## 1     1 1 nonlowfat atrest      85 min01
## 2     1 1 nonlowfat atrest      85 min15
## 3     1 1 nonlowfat atrest      88 min30
## 4     2 2 nonlowfat atrest      90 min01
## 5     2 2 nonlowfat atrest      92 min15
## 6     2 2 nonlowfat atrest      93 min30
## 7     3 3 nonlowfat atrest      97 min01
## 8     3 3 nonlowfat atrest      97 min15
```

- This is “long format”, which is usually what we want.
- But for repeated measures analysis, we want *wide* format!
- “undo” gather: spread.

Making wide format

- spread needs: a column that is going to be split, and the column to make the values out of:

```
exercise.long %>% spread(time, pulse) -> exercise.wide
exercise.wide %>% sample_n(5)
```

```
## # A tibble: 5 x 6
##       id diet      exertype min01 min15 min30
##   <dbl> <chr>    <chr>    <dbl> <dbl> <dbl>
## 1    17 lowfat    walking    103    109    90
## 2    27 lowfat    running    100    126   140
## 3     7 lowfat    atrest      87     88    90
## 4     1 nonlowfat atrest      85     85    88
## 5     6 lowfat    atrest      83     83    84
```

- Normally gather min01, min15, min30 into one column called pulse labelled by the number of minutes. But Manova needs it the other way.

Setting up the repeated-measures analysis

- Make a response variable consisting of min01, min15, min30:

```
response <- with(exercise.wide, cbind(min01, min15, min30))
```

- Predict that from diet and exertype and interaction using lm:

```
exercise.1 <- lm(response ~ diet * exertype,
  data = exercise.wide
)
```

- Run this through Manova:

```
times <- colnames(response)
times.df <- data.frame(times)
exercise.2 <- Manova(exercise.1,
  idata = times.df,
  idesign = ~times)
```

Results

```
exercise.2
```

```
##
## Type II Repeated Measures MANOVA Tests: Pillai test statistic
##
```

	Df	test	stat	approx	F	num	Df	den	Df	Pr(>F)
## (Intercept)	1	0.99767	10296.7			1	24	< 2.2e-16		***
## diet	1	0.37701	14.5			1	24	0.0008483		***
## exertype	2	0.79972	47.9			2	24	4.166e-09		***
## diet:exertype	2	0.28120	4.7			2	24	0.0190230		*
## times	1	0.78182	41.2			2	23	2.491e-08		***
## diet:times	1	0.25153	3.9			2	23	0.0357258		*
## exertype:times	2	0.83557	8.6			4	48	2.538e-05		***
## diet:exertype:times	2	0.51750	4.2			4	48	0.0054586		**

```
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

- Three-way interaction significant, so cannot remove anything.
- Pulse rate depends on diet and exercise type *combination*, and *that* is different for each time.

Making some graphs

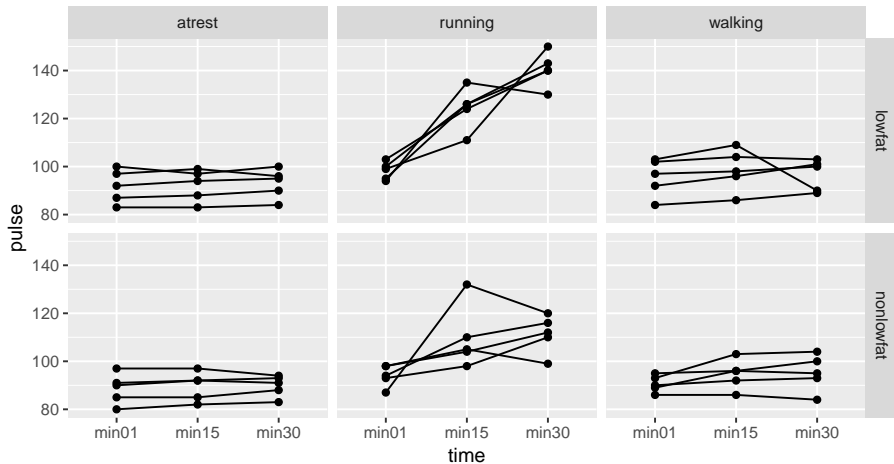
- Three-way interactions are difficult to understand. To make an attempt, look at some graphs.
- Plot time trace of pulse rates for each individual, joined by lines, and make *separate* plots for each diet-exertype combo.
- ggplot again. Using *long* data frame:

```
g <- ggplot(exercise.long, aes(
  x = time, y = pulse,
  group = id
)) + geom_point() + geom_line() +
  facet_grid(diet ~ exertype)
```

- `facet_grid(diet~exertype)`: do a separate plot for each combination of diet and exercise type, with diets going down the page and exercise types going across. (Graphs are usually landscape, so have the factor `exertype` with more levels going across.)

The graph(s)

g



Comments on graphs

- For subjects who were at rest, no change in pulse rate over time, for both diet groups.
- For walking subjects, not much change in pulse rates over time. Maybe a small increase on average between 1 and 15 minutes.
- For both running groups, an overall increase in pulse rate over time, but the increase is stronger for the lowfat group.
- No consistent effect of diet over all exercise groups.
- No consistent effect of exercise type over both diet groups.
- No consistent effect of time over all diet-exercise type combos.

“Simple effects” of diet for the subjects who ran

- Looks as if there is only any substantial time effect for the runners. For them, does diet have an effect?
- Pull out only the runners from the wide data:

```
exercise.wide %>%
  filter(exertype == "running") -> runners.wide
```

- Create response variable and do MANOVA. Some of this looks like before, but I have different data now:

```
response <- with(runners.wide, cbind(min01, min15, min30))
runners.1 <- lm(response ~ diet, data = runners.wide)
times <- colnames(response)
times.df <- data.frame(times)
runners.2 <- Manova(runners.1,
  idata = times.df,
  idesign = ~times
)
```

Results

```
runners.2
```

```
##
## Type II Repeated Measures MANOVA Tests: Pillai test statistic
##          Df test stat approx F num Df den Df      Pr(>F)
## (Intercept) 1    0.99912   9045.3      1      8 1.668e-13 ***
## diet         1    0.84986    45.3      1      8 0.0001482 ***
## times        1    0.92493    43.1      2      7 0.0001159 ***
## diet:times   1    0.68950     7.8      2      7 0.0166807 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

text under

- The diet by time interaction is still significant (at $\alpha = 0.05$): the effect of time on pulse rates is different for the two diets.
- At $\alpha = 0.01$, the interaction is not significant, and then we have only two (very) significant main effects of diet and time.

How is the effect of diet different over time?

- Table of means. Only I need long data for this, so make it (in a pipeline):

```
runners.wide %>%
  gather(time, pulse, min01:min30) %>%
  group_by(time, diet) %>%
  summarize(
    mean = mean(pulse),
    sd = sd(pulse)
  ) -> summ
```

- Result of `summarize` is data frame, so can save it (and do more with it if needed).

Understanding diet-time interaction

- The summary:

```
summ
```

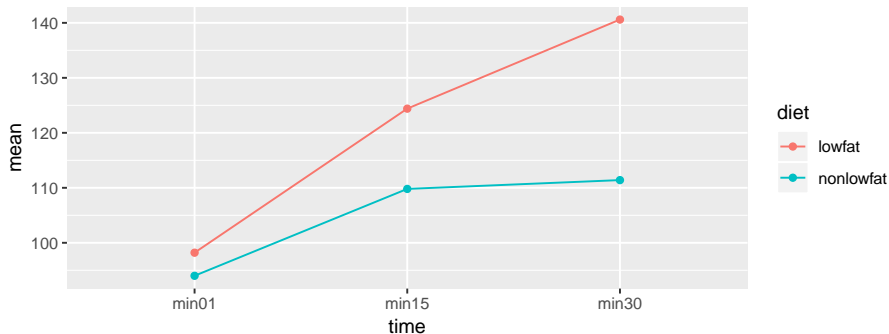
```
## # A tibble: 6 x 4
## # Groups:   time [3]
##   time diet      mean    sd
##   <chr> <chr>    <dbl> <dbl>
## 1 min01 lowfat    98.2  3.70
## 2 min01 nonlowfat  94    4.53
## 3 min15 lowfat   124.   8.62
## 4 min15 nonlowfat 110.  13.1
## 5 min30 lowfat   141.   7.20
## 6 min30 nonlowfat 111.   7.92
```

- Pulse rates at any given time higher for lowfat (diet effect),
- Pulse rates increase over time of exercise (time effect),
- but the *amount by which pulse rate higher* for a diet depends on time: diet by time interaction.

Interaction plot

- We went to trouble of finding means by group, so making interaction plot is now mainly easy:

```
ggplot(summ, aes(x = time, y = mean, colour = diet,  
                 group = diet)) + geom_point() + geom_line()
```



Comment on interaction plot

- The lines are not parallel, so there is interaction between diet and time for the runners.
- The effect of time on pulse rate is different for the two diets, even though all the subjects here were running.