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Week 3 — Multiple linear regression, transformations, and model building

Introduction to Statistical Thinking and Data Analysis
MSc in Epidemiology / Health Data Analytics
Autumn 2022

24 October 2022

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This week

Time	Session	Topic
Mon 24 Oct 9:30–10:30	Problem Set Review	Problem Set 2: Linear regression
Mon 24 Oct 10:45–12:30	Lecture	Multiple linear regression, transformations, and model building
Mon 24 Oct 13:30–15:30	Applied Statistics Lab	Project 1: performing the analysis
Wed 26 Oct 9:30–11:00	Small group tutorial (Epi)	Problem Set 3
Wed 26 Oct 15:30–17:00	Small group tutorial (HDA)	Problem Set 3

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Announcements

- We plan to start posting email questions + responses also on Blackboard discussion board when they may be of wider interest
- We will aim to post problem set solutions at end of Friday (instead of Sunday)
- Working on creating annotated R script examples for problem set solutions

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Learning objectives

- Define and interpret the correlation coefficient r and r^2, and understand the difference between the correlation coefficient and regression coefficient.
- Use multiple regression to describe, to adjust, and to predict.
- Interpret interactions and decide when to include interaction terms in multiple regression.
- Know why and when to transform outcome and exposure variables in linear regression.
- Develop a model building strategy to identify which and how many variables to include in a model.

Readings

- Kirkwood and Sterne:
  - Chapter 10: Linear regression and correlation
  - Chapter 11: Multiple regression
  - Chapter 12: Regression diagnostics
  - Chapter 13: Transformations
  - Chapter 29: Regression modelling
    - Sections 29.5, 29.7, 29.8
  - Chapter 38: Strategies for analysis
    - Sections 38.5–38.8

Analysis of Variance (ANOVA)

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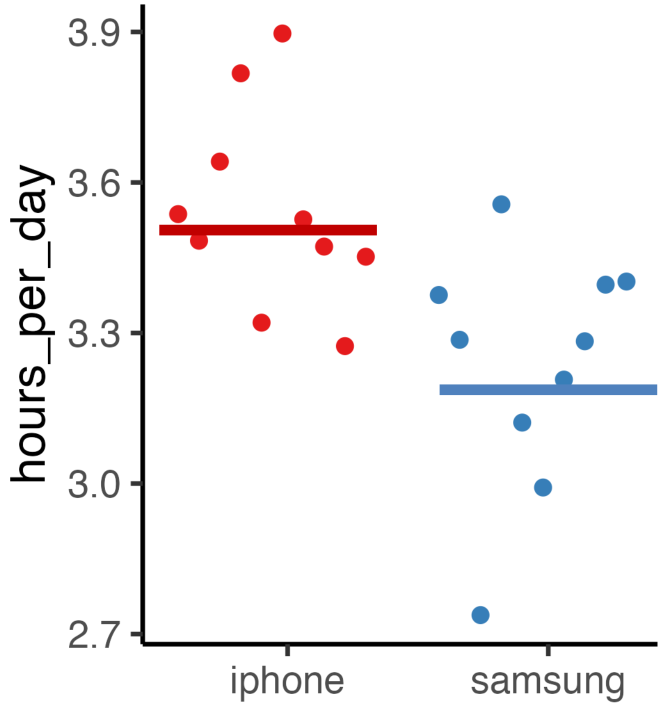
Analysis of variance

How many hours per day do users of different phone manufacturers spend on TikTok?

- Sample n = 10 iPhone users and n = 10 Samsung users

	Mean
iPhone	3.54
Samsung	3.24

- Difference: 0.3
- Pooled SE: 0.097
- t-statistic: 3.149 on 18 degrees of freedom
- p-value: 0.005



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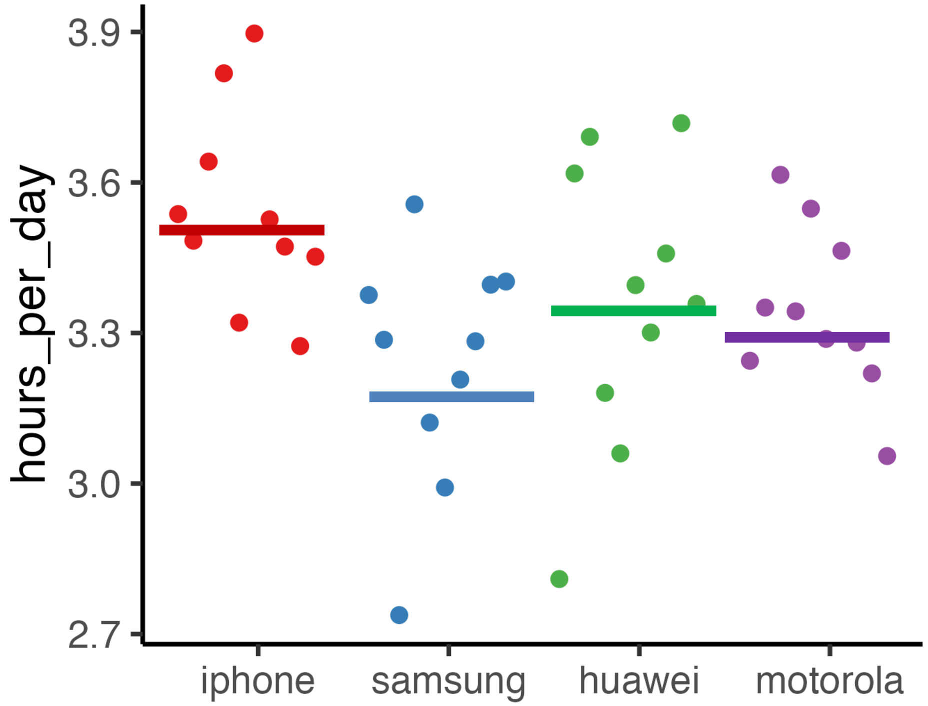
Analysis of variance

Is the mean number of hours per day on TikTok different by users of different leading phone manufacturers?

- Sample n = 10 of each iPhone, Samsung, Huawei, and Motorola users



Mean hours per day:	3.54 hr	3.24 hr	3.36 hr	3.34 hr

Option: Linear regression w/ categorical

```
> summary(lm(hours_per_day ~ manufacturer, data = phones))

Call:
lm(formula = hours_per_day ~ manufacturer, data = phones)

Residuals:
     Min       1Q   Median       3Q      Max 
-0.54936 -0.10078 -0.00318  0.14492  0.35915 

Coefficients:
                     Estimate Std. Error t value Pr(>|t|)    
(Intercept)           3.54223    0.07151  49.538  < 2e-16 ***
manufacturersamsung  -0.30628    0.10112  -3.029  0.00452 ** 
manufacturerhuawei   -0.18321    0.10112  -1.812  0.07837 .  
manufacturermotorola -0.20136    0.10112  -1.991  0.05408 .  
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2261 on 36 degrees of freedom
Multiple R-squared:  0.2089,	Adjusted R-squared:  0.143 
F-statistic: 3.168 on 3 and 36 DF,  p-value: 0.03594
```

- Informs about mean hours per day vs. iPhone users
- Does not answer question is there a difference in the mean across all four groups

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Analysis of variance

Is the mean number of hours per day on TikTok different by users of different leading phone manufacturers?

$$s^2 = \frac{SS}{df} = \frac{\sum(x-\bar{x})^2}{n-1}$$

- Decompose the variance & degrees of freedom:

Group: squared differences between group mean and overall population mean

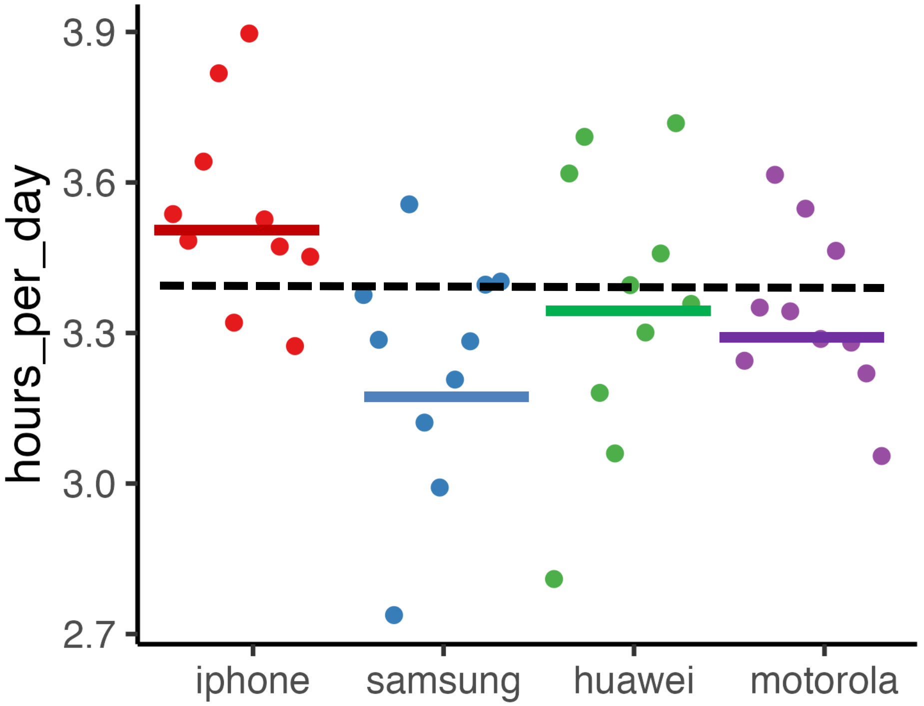
$$s^2 = \frac{SS}{df} = \frac{SS_{\text{group}} + SS_{\text{res}}}{df_{\text{group}} + df_{\text{res}}}$$

Residual: difference between each observation and group mean

sum squares/df

	Sum Sq.	d.f.	Mean Sq.
Group	0.486	4 groups - 1 3	0.162
Residual	1.841	36	0.051
Total	2.327	39	

Sample n = 10 of each iPhone, Samsung, Huawei, and Motorola users



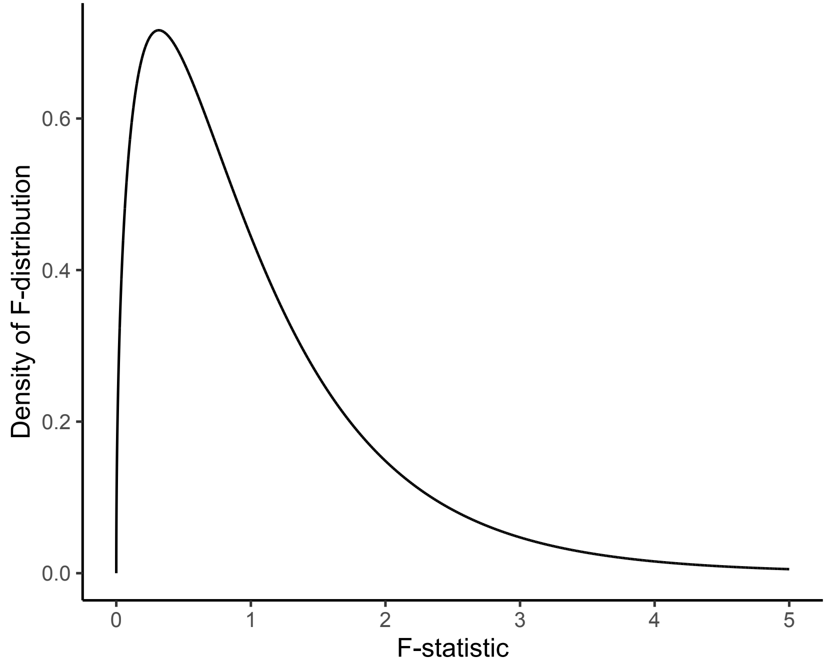
Mean hours per day: **3.54 hr** **3.24 hr** **3.36 hr** **3.34 hr**

F-statistic

$$F = \frac{\text{Between-group mean square}}{\text{Within-group (residual) mean square}}$$

- With degrees of freedom:
  - df1 = between-group d.f.
  - df2 = within-group d.f. residual group freedomo
- *Assuming null hypothesis that all means are equal*, F-statistic follows an F-distribution
- P-value based on tail of the F-disitribution

F-distribution with df_1=3 and df_2=36 degrees of freedom



	Sum Sq.	d.f.	Mean Sq.	F-stat	p-value
Group	0.486	3	0.162	3.168	0.0356
Residual	1.841	36	0.051		
Total	2.327	39			

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F-test in R

```
> fit <- lm(hours_per_day ~ manufacturer, data = phones)

> anova(fit)

Analysis of Variance Table

Response: hours_per_day
             Df Sum Sq Mean Sq F value  Pr(>F)
manufacturer  3 0.4860 0.16200  3.1684 0.03594 *
Residuals    36 1.8407 0.05113
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

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ANOVA in linear regression output

```
Call:
lm(formula = hours_per_day ~ manufacturer, data = phones)

Residuals:
     Min       1Q   Median       3Q      Max 
-0.54936 -0.10078 -0.00318  0.14492  0.35915 

Coefficients:
                     Estimate Std. Error t value Pr(>|t|)    
(Intercept)           3.54223    0.07151  49.538  < 2e-16 ***
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manufacturerhuawei   -0.18321    0.10112  -1.812  0.07837 .  
manufacturermotorola -0.20136    0.10112  -1.991  0.05408 .  
---
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Residual standard error: 0.2261 on 36 degrees of freedom
Multiple R-squared:  0.2089,	Adjusted R-squared:  0.143 
F-statistic: 3.168 on 3 and 36 DF,  p-value: 0.03594
```

same as anova output

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Correlation and coefficient of determination (R^2)

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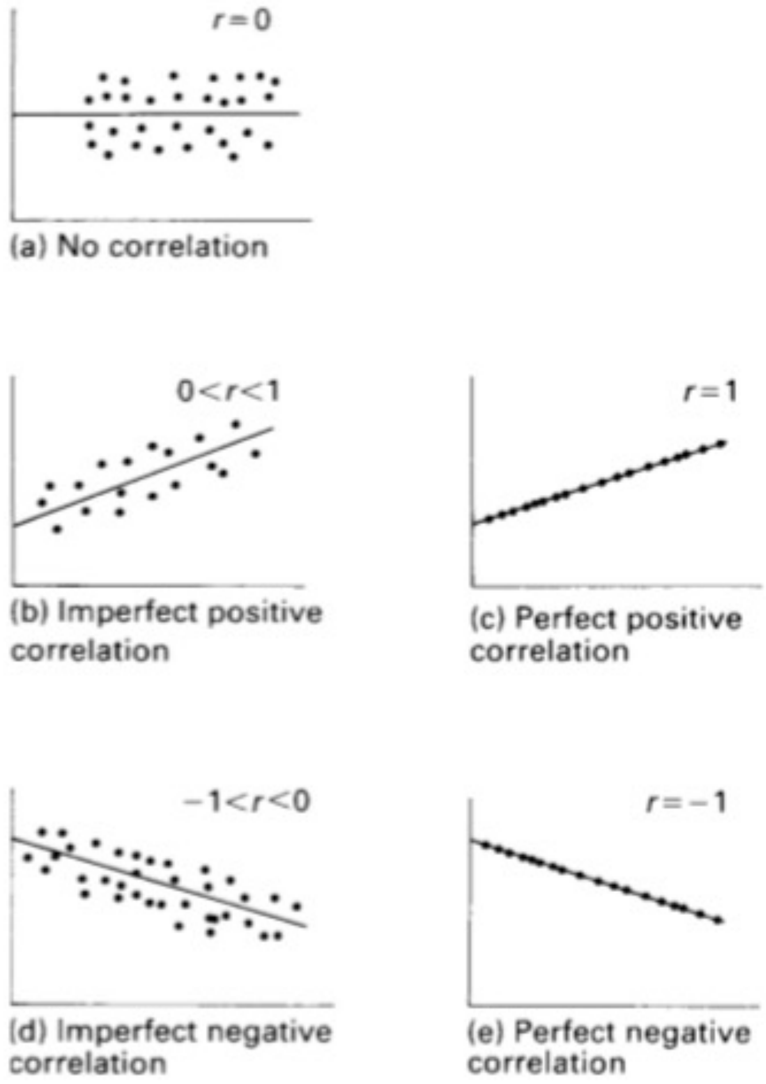
Correlation coefficient

- Regression coefficient (β_1): average change in outcome y for a one unit change in x.
  - Depends on the units of x and y

- Correlation coefficient (r): *strength* of linear association between two variables.
  - Number of standard deviations that y changes for each standard deviation change in x.

- r is between -1 and 1
  - $r = 0$ → no correlation; regression slope also = 0
  - $0 < r < 1$ → positive correlation; $\beta_1 > 0$
  - $-1 < r < 0$ → negative correlation; $\beta_1 < 0$

- Two datasets can have the same β_1, but different r.
  - More spread around the regression line → lower absolute correlation.
  - If we standardize x and y, then $\beta_1 = r$
  - But uncommon; usually most interested in interpreting β_1 on natural scale.



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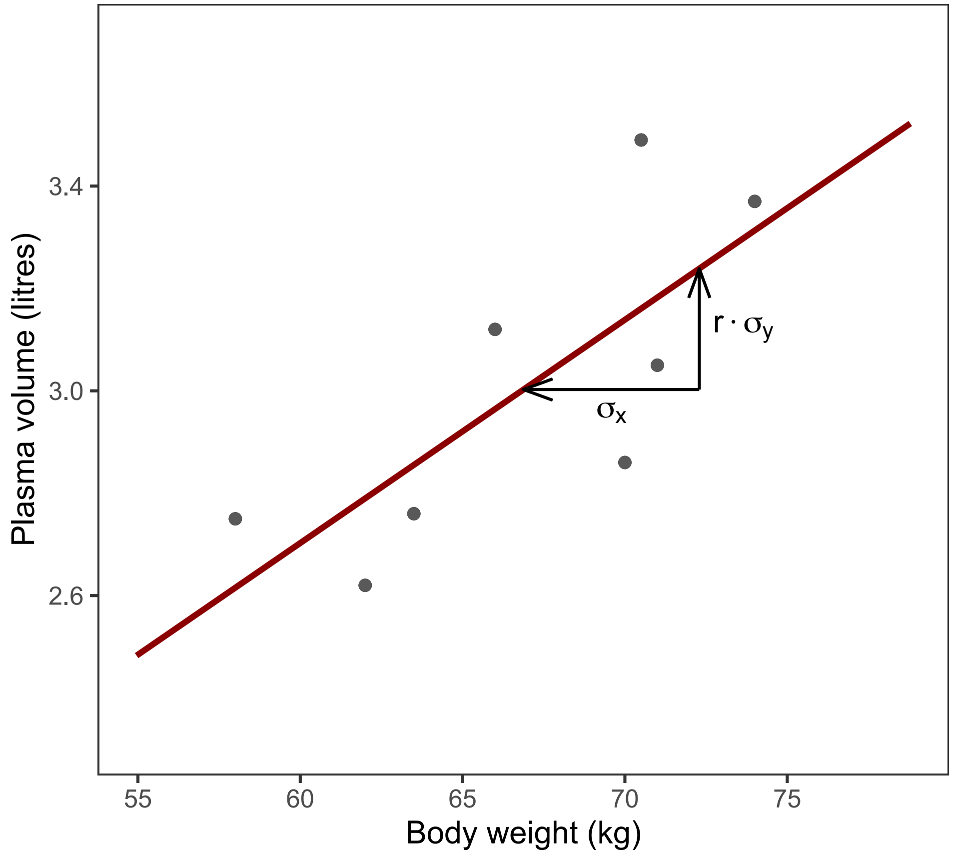
Correlation coefficient

Subject	Weight (kg)	Plasma volume (L)
1	58.0	2.75
2	70.0	2.86
3	74.0	3.37
4	63.5	2.76
5	62.0	2.62
6	70.5	3.49
7	71.0	3.05
8	66.0	3.12



mean(Weight) = 66.88 SD(Weight) = 5.42
mean(Plasma) = 3.003 SD(Plasma) = 0.311
$r = 0.759$

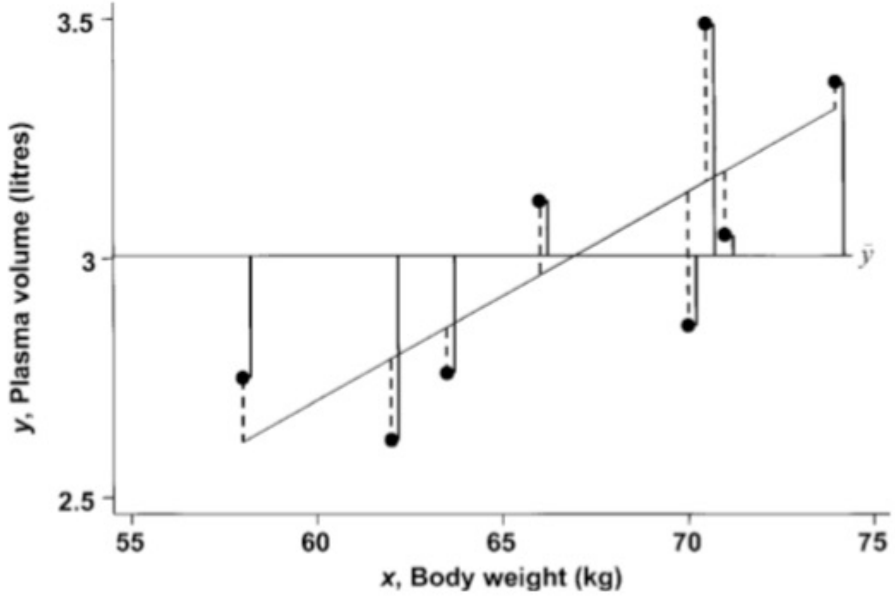
Plasma = 0.0857 + 0.0436 * Weight
SD(Weight) * β_1 = 5.42 * 0.0436 = 0.236
SD(Plasma) * r = 0.311 * 0.759 = 0.236

Coefficient of determination

- **Coefficient of determination—$\boldsymbol{R^2}$:** measures of the proportion of the total variation in the data that has been explained by the regression.
  - Always between 0 and 1.

- Defined by Analysis of Variance (ANOVA):

$$R^2 = \frac{SS_{Total} - SS_{Residual}}{SS_{Total}} = \frac{SS_{Regression}}{SS_{Total}}$$



- For simple linear regression, coefficient of determination is equal to square of correlation (r^2).

- R^2 is distinct from hypothesis testing for regression coefficients.
  - High / low R^2 does not mean a model is 'good'/'bad'; they R^2 and inference for β's answer different questions.

Correlation in R

```
> dat <- data.frame(subject = 1:8,
                    weight = c(58, 70, 74, 63.5,
                               62, 70.5, 71, 66),
                    plasma = c(2.75, 2.86, 3.37, 2.76,
                               2.62, 3.49, 3.05, 3.12))

> x <- dat$weight
> y <- dat$plasma
> xbar <- mean(x)
> ybar <- mean(y)

> r <- sum((x - xbar) * (y - ybar)) /
+       sqrt(sum((x-xbar)^2) * sum((y - ybar)^2))
> r
[1] 0.7591266

> cor(dat$weight, dat$plasma)
[1] 0.7591266

## Coefficient of determination
> r^2
[1] 0.5762732
```

```
> summary(lm(plasma ~ weight, data = dat))

Call:
lm(formula = plasma ~ weight, data = dat)

Residuals:
     Min       1Q   Median       3Q      Max
-0.27880 -0.14178 -0.01928  0.13986  0.32939

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  0.08572    1.02400   0.084   0.9360
weight       0.04362    0.01527   2.857   0.0289 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '
1

Residual standard error: 0.2188 on 6 degrees of freedom
Multiple R-squared:  0.5763,    Adjusted R-squared:  0.5057
F-statistic:  8.16 on 1 and 6 DF,  p-value: 0.02893
```

- Body weight accounts for 57.6% of the total variation in plasma volume.

interpretation of r2

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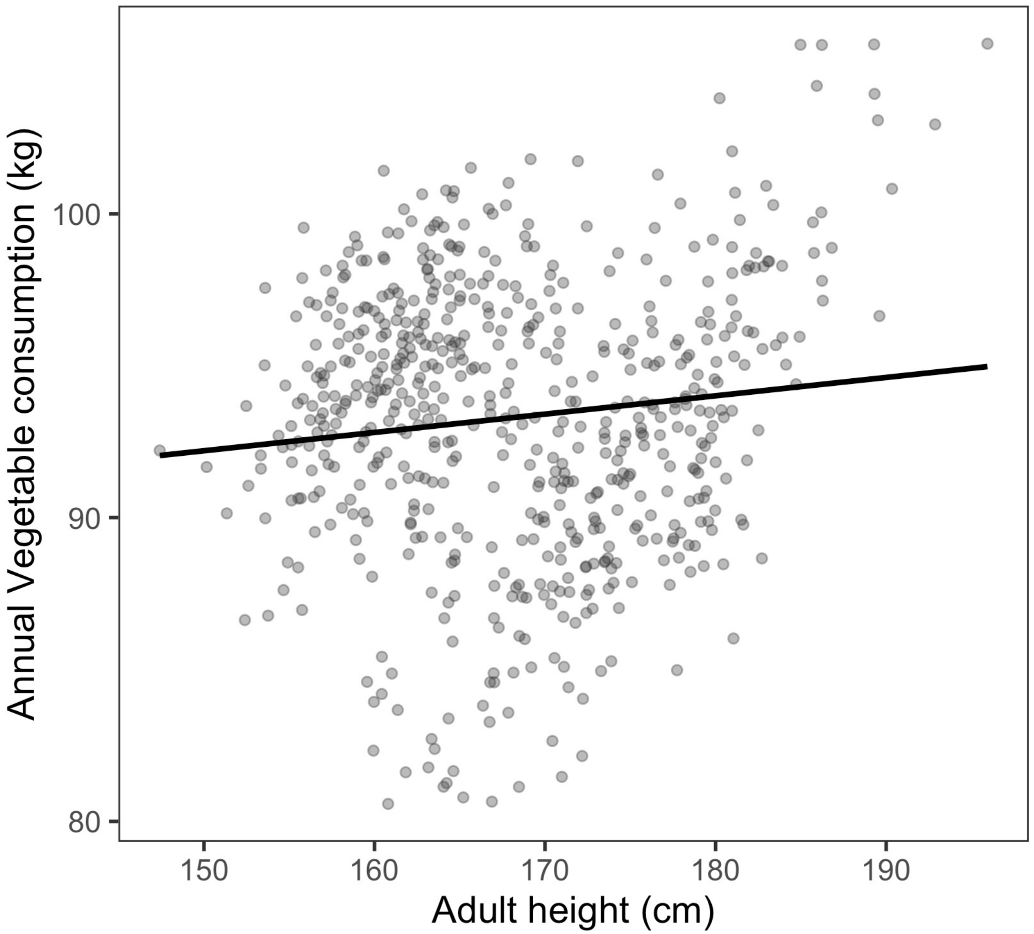
Multiple linear regression

Example: height and vegetable consumption

<u>Data:</u> random sample of 600 adults in the UK

$$\text{Veg cons.} = \beta_0 + \beta_{height} \times \text{height} + \epsilon$$



Param.	Estim.	Std. err.	t-value	p-value	95% CI
β_0	83.1503	3.6202	22.97	<0.001	(76.04–99.26)
β_{height}	0.0603	0.0214	2.81	0.005	(0.018–0.103)
R^2	0.013				

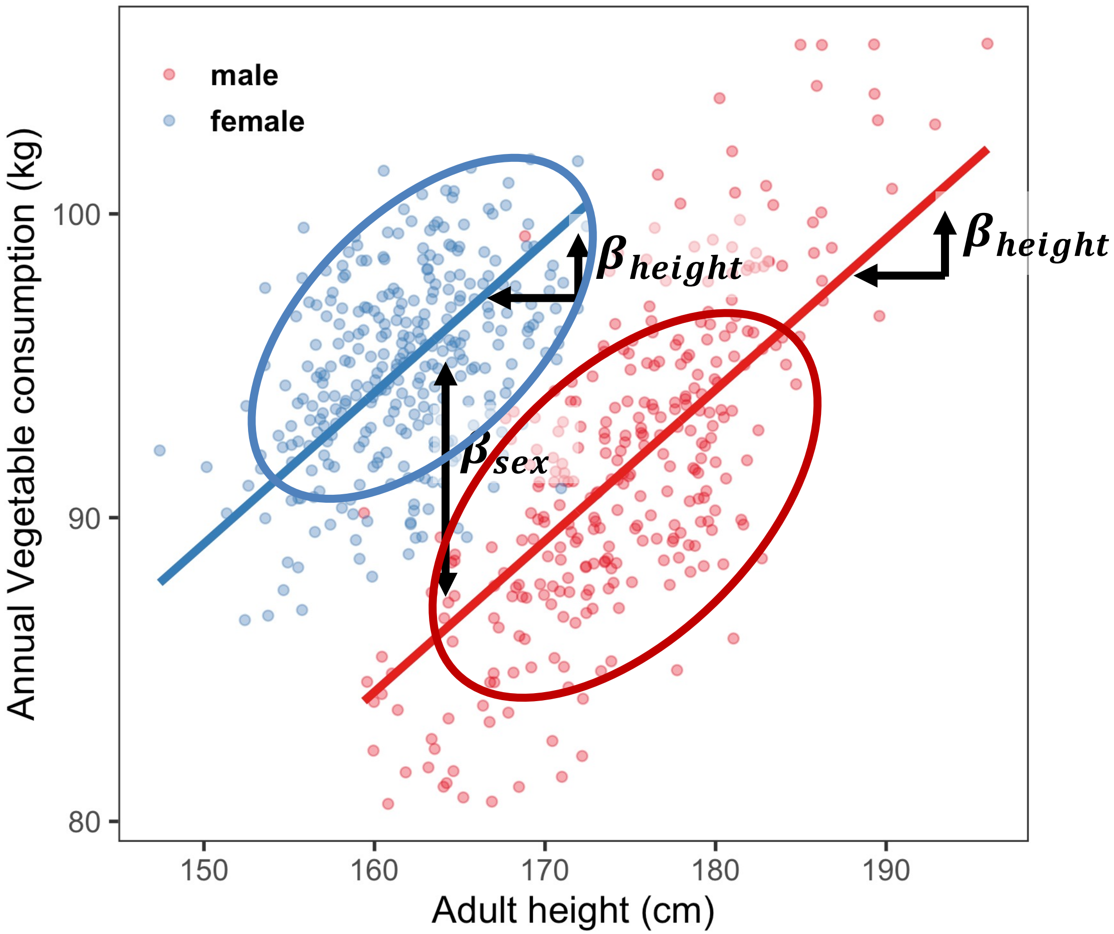
Among population of adults in the UK:

- On average, consume 60g (0.06 kg) more vegetables each year per 1 cm taller height; 95% CI 18g to 103g.
- Strong evidence to **reject** null hypothesis of no association between vegetable consumption and height.
- Height explains about 1.3% of variation in vegetable consumption.

statistically significant relationship

Example: height and vegetable consumption

Data: random sample of 600 adults in the UK
- 300 men, 300 women



$$\text{Veg cons.} = \beta_0 + \beta_{sex}\times[\text{sex} = \text{F}] + \beta_{height}\times\text{height} + \epsilon$$

Param.	Estim.	Std. err.	t-value	p-value	95% CI
β_0	4.669	4.136	1.129	0.259	(-3.45–12.79)
β_{sex}	9.854	0.407	24.237	<0.001	(9.06–10.65)
β_{height}	0.497	0.024	21.052	<0.001	(0.451–0.544)
R^2	0.503				

Among population of adults in the UK:
- Women eat around 9.9kg more vegetables per year, *adjusted for height* (95% CI 9.1–10.7kg)
- Additional 1 cm height associated with 498g (95% CI 451–544g) more veg consumption, adjusted for sex.
- Sex and height explain about 50% of the variation in annual vegetable consumption.

Multiple linear regression

- Examine dependency of outcome on **<u>several</u>** exposure variables, not just one.

- Two reasons for including additional exposure variables:
  1. Estimate an exposure effect after accounting for the effect of other variables—adjusting for ***confounding*** factors.
     - Example: *Women were on average shorter and ate more vegetables than men of similar height→ sex **confounded** the relationship between height and vegetable consumption*
  2. Systematically explain additional variation in the data → reduce residual variation → decrease standard error of regression coefficient
     - Increases accuracy of coefficient estimate; likelihood that hypothesis will detect any real effect that exists
     - Only applies to linear regression (not, e.g., logistic or Poisson regression)

- *What is the association between vegetable consumption and height, adjusted for effect of sex?*
- *What is the association between vegetable consumption and sex, adjusted for effect of height?*
  - ‘adjusted for’ = having taken into account
  - Also often referred to as ‘controlled for’; ‘adjusted for’ generally preferred language now.

Multiple regression in R

Simple linear regression

```
> fit1 <- lm(veg ~ height, data = dat)

> summary(fit1)

Call:
lm(formula = veg ~ height, data = dat)

Residuals:
     Min       1Q   Median       3Q      Max
-12.5693  -2.9901   0.3621   3.2112  11.2556

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 83.15026    3.62024  22.968  < 2e-16 ***
height       0.06034    0.02149   2.808  0.00514 **

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

Residual standard error: 4.528 on 598 degrees of freedom
Multiple R-squared:  0.01302,    Adjusted R-squared:  0.01137
F-statistic: 7.887 on 1 and 598 DF,  p-value: 0.005143
```

Multiple linear regression

```
> fit2 <- lm(veg ~ sex + height, data = dat)

> summary(fit2)

Call:
lm(formula = veg ~ sex + height, data = dat)

Residuals:
    Min      1Q  Median      3Q     Max
-8.7129 -2.2744  0.1207  2.1465 10.6118

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  4.66867    4.13555   1.129    0.259
sexfemale    9.85417    0.40658  24.237   <2e-16 ***
height       0.49747    0.02363  21.052   <2e-16 ***
---
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 3.217 on 597 degrees of freedom
Multiple R-squared:  0.5025,     Adjusted R-squared:  0.5008
F-statistic: 301.5 on 2 and 597 DF,  p-value: < 2.2e-16
```

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Comparing multiple regression models

- Use ANOVA to test the null hypothesis that no association of veg consumption with sex, having already accounted for height.

- Reverse order: null hypothesis no association of veg consumption and height, having already accounted for sex.

Notes:

- Models must be ‘nested’
  - All terms in model 1 must also be included in model 2
- For single additional variable, equivalent to t-test for the added term in multiple regression table.
  - t-statistic is square-root of the F-statistic
- More useful for categorical variables (multiple levels)
  - H0: all of the additional categories are = 0
  - H1: at least one of additional categories != 0

```
> fit1a <- lm(veg ~ height, data = dat)
> fit2 <- lm(veg ~ height + sex, data = dat)

> anova(fit1a, fit2)
Analysis of Variance Table

Model 1: veg ~ height
Model 2: veg ~ height + sex
  Res.Df     RSS Df Sum of Sq      F    Pr(>F)
1    598 12260.0
2    597  6179.7  1    6080.4 587.41 < 2.2e-16 ***
---
```

```
> fit1b <- lm(veg ~ sex, data = dat)
> fit2 <- lm(veg ~ sex + height, data = dat)
> anova(fit1b, fit2)
```

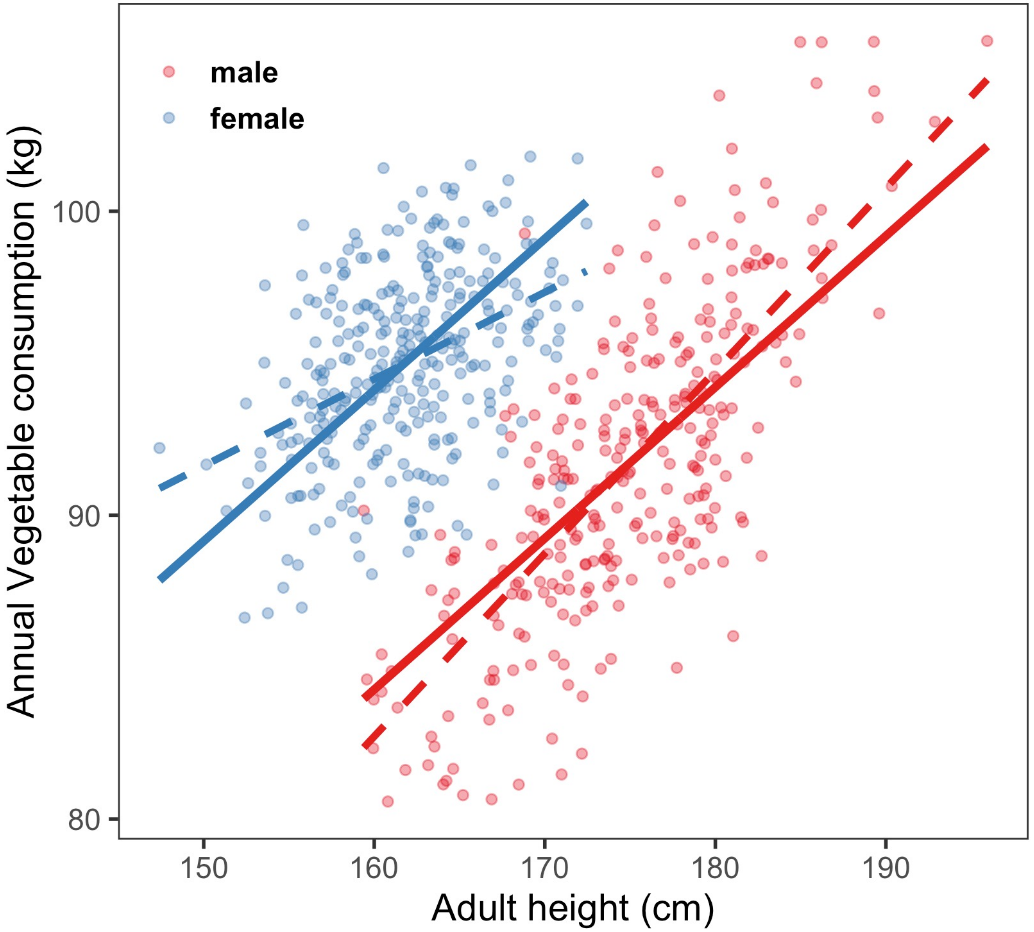
compares model 1 and 2

```
Analysis of Variance Table

Model 1: veg ~ sex
Model 2: veg ~ sex + height
  Res.Df     RSS Df Sum of Sq      F    Pr(>F)
1    598 10767.2
2    597  6179.7  1    4587.6 443.19 < 2.2e-16 ***
---
```

Interactions

Is the relationship between height and vegetable consumption different for women and men?



$$\text{Veg cons.} = \beta_0 + \beta_{sex} \times [\text{sex} = \text{F}] + \beta_{height} \times \text{height} + \beta_{sexF,height} \times [\text{sex} = \text{F}] \times \text{height} + \epsilon$$

Param.	Estim.	Std. err.	t-value	p-value	95% CI
β_0	-13.503	4.882	-2.766	0.006	(-23.09– -3.91)
β_{sex}	62.272	8.085	7.703	<0.001	(46.39–78.15)
β_{height}	0.601	0.028	21.551	<0.001	(0.547–0.656)
$\beta_{sexF,height}$	-0.316	0.049	-6.491	<0.001	(-0.411– -0.220)
R^2	0.535				

- $\beta_{sexF,height}$: is the effect of the *interaction* between sex and height
  - Also called *effect modification*: sex modifies the effect of height on vegetable consumption.

Interactions

$$\text{Veg cons.} = \beta_0 + \beta_{sex} \times [\text{sex} = \text{F}] + \beta_{height} \times \text{ height} + \beta_{sexF,height} \times [\text{sex} = \text{F}] \times \text{height} + \epsilon$$

Param.	Estim.	Std. err.	t-value	p-value	95% CI
β_0	-13.503	4.882	-2.766	0.006	(-23.09– -3.91)
β_{sex}	62.272	8.085	7.703	<0.001	(46.39–78.15)
β_{height}	0.601	0.028	21.551	<0.001	(0.547–0.656)
$\beta_{sexF,height}$	-0.316	0.049	-6.491	<0.001	(-0.411– -0.220)
R^2	0.535				

- β_0: The predicted vegetable consumption for *men* with *height = 0cm* is -13.5kg per year.
- β_{sex}: The predicted difference between female veg consumption and male veg consumption is 62.3kg per year <u>when height = 0</u> (for both sexes)
- β_{height}: <u>For men,</u> vegetable consumption increases by 0.6kg for each cm height.
- $\beta_{sexF,height}$: <u>For women,</u> each cm increase in height is associated with <u>**0.32kg less increase**</u> in veg consumption than for men.
  - <u>For women,</u> vegetable consumption increases by 0.60 - 0.32 = 0.28 kg per cm increase in height

check updated slide deck

Interactions in R

Multiple regression with interaction

```
> fit3 <- lm(veg ~ sex + height + sex:height, data = dat)

> summary(fit1)

Call:
lm(formula = veg ~ height, data = dat)

Residuals:
     Min       1Q   Median       3Q      Max 
-12.5693  -2.9901   0.3621   3.2112  11.2556 

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 83.15026    3.62024  22.968  < 2e-16 ***
height       0.06034    0.02149   2.808  0.00514 **

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

Residual standard error: 4.528 on 598 degrees of freedom
Multiple R-squared:  0.01302,    Adjusted R-squared:  0.01137
F-statistic: 7.887 on 1 and 598 DF,  p-value: 0.005143
```

Multiple linear regression

```
> fit2 <- lm(veg ~ sex + height, data = dat)

> summary(fit2)

Call:
lm(formula = veg ~ sex + height, data = dat)

Residuals:
    Min      1Q  Median      3Q     Max 
-8.7129 -2.2744  0.1207  2.1465 10.6118 

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  4.66867    4.13555   1.129    0.259
sexfemale    9.85417    0.40658  24.237   <2e-16 ***
height       0.49747    0.02363  21.052   <2e-16 ***
---
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 3.217 on 597 degrees of freedom
Multiple R-squared:  0.5025,    Adjusted R-squared:  0.5008
F-statistic: 301.5 on 2 and 597 DF,  p-value: < 2.2e-16
```

NB: `lm(veg ~ sex + height + sex:height, ...)` and `lm(veg ~ sex*height, ...)` are equivalent.

Centering covariates

only include if there's a clear motivation behind why the confounder could affect

- Often 'centering' covariates at their mean makes results more interpretable.
  - E.g.: height = 0 -> height = mean(height)

```
> mean(dat$height)
[1] 168.2679
> dat$height_c <- dat$height - mean(dat$height)

> fit3_c <- lm(veg ~ sex + height_c + sex:height_c, data=dat)

Call:
lm(formula = veg ~ sex + height_c + sex:height_c, data = dat)

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
(Intercept)       87.69415    0.25663 341.720  < 2e-16 ***
sexfemale          9.14602    0.40811  22.411  < 2e-16 ***
height_c           0.60141    0.02791  21.551  < 2e-16 ***
sexfemale:height_c -0.31572   0.04864  -6.491 1.79e-10 ***
---

Residual standard error: 3.112 on 596 degrees of freedom
Multiple R-squared:  0.5354,    Adjusted R-squared:  0.533
F-statistic: 228.9 on 3 and 596 DF,  p-value: < 2.2e-16
```

- Estimate for `height` slope, `sexfemale:height` interaction, R^2, and statistical inferences are unchanged.

- Intercept and sex coefficients are more interpretable:
  - β_0: The predicted vegetable consumption for *men* with *height = 168cm* is 87.7kg per year.
  - β_{sex}: For men and women both with height = 168cm, women consume 9.1kg more vegetables per year than men.

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Interaction of continuous covariates

Peru lung function data set (636 children aged 7 to 10 years)

- Estimate interaction between effect of height and age on lung function (FEV1)

```
> peru_fit <- lm(fev1 ~ age*height, peru)

> summary(peru_fit)

Call:
lm(formula = fev1 ~ age * height, data = peru)

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept)  3.793279   1.956125   1.939  0.05292 .
age         -0.587443   0.216724  -2.711  0.00690 **
height      -0.024679   0.015950  -1.547  0.12230
age:height   0.005497   0.001755   3.133  0.00181 **
---
Signif. codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2275 on 632 degrees of freedom
Multiple R-squared:  0.4442,    Adjusted R-squared:  0.4416
F-statistic: 168.4 on 3 and 632 DF,  p-value: < 2.2e-16
```

- *For every 1 year older age*, the effect of an additional cm of height on FEV1 is increased by 0.005 L/sec

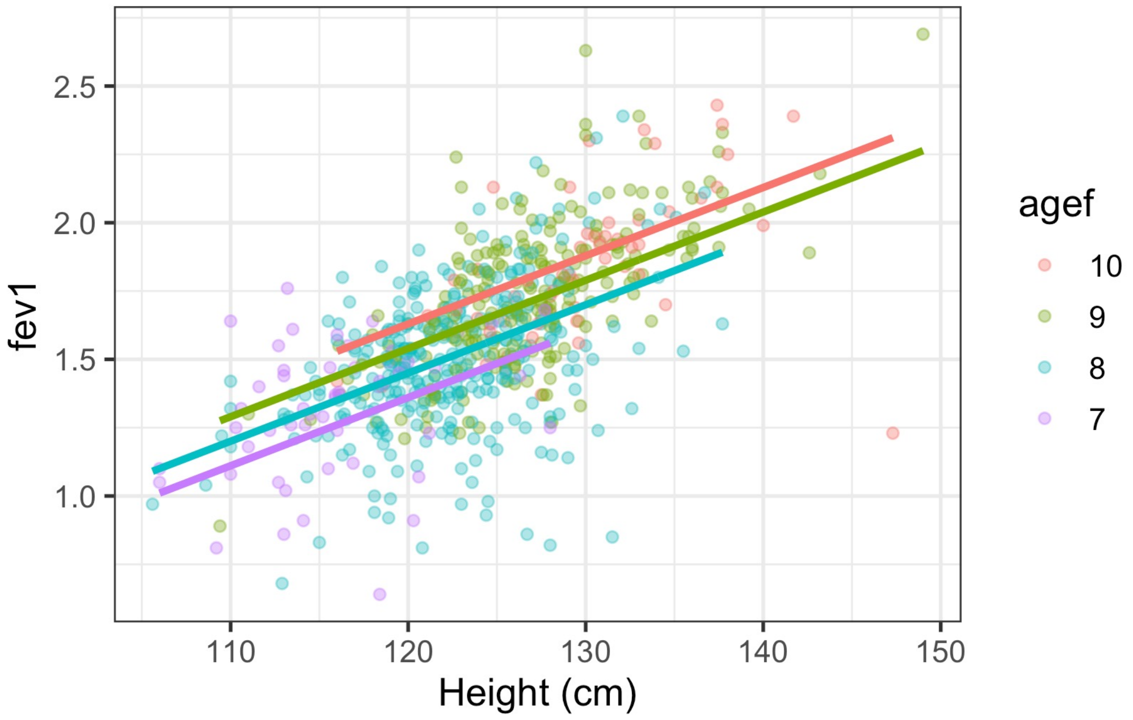
- *For each cm additional height*, the effect of an additional year of age on FEV1 is increased by 0.005 L/sec

- Often useful / clearer to communicate slopes for indicative values:
  - At age 7, each ⬆ cm height **0.016 L/sec** ⬆ FEV1
  - At age 8, each ⬆ cm height -> **0.022 L/sec** ⬆ FEV1
  - At age 9, each ⬆ cm height -> **0.028 L/sec** ⬆ FEV1
  - At age 10, each ⬆ cm height -> **0.033 L/sec** ⬆ FEV1

Interaction of continuous covariates

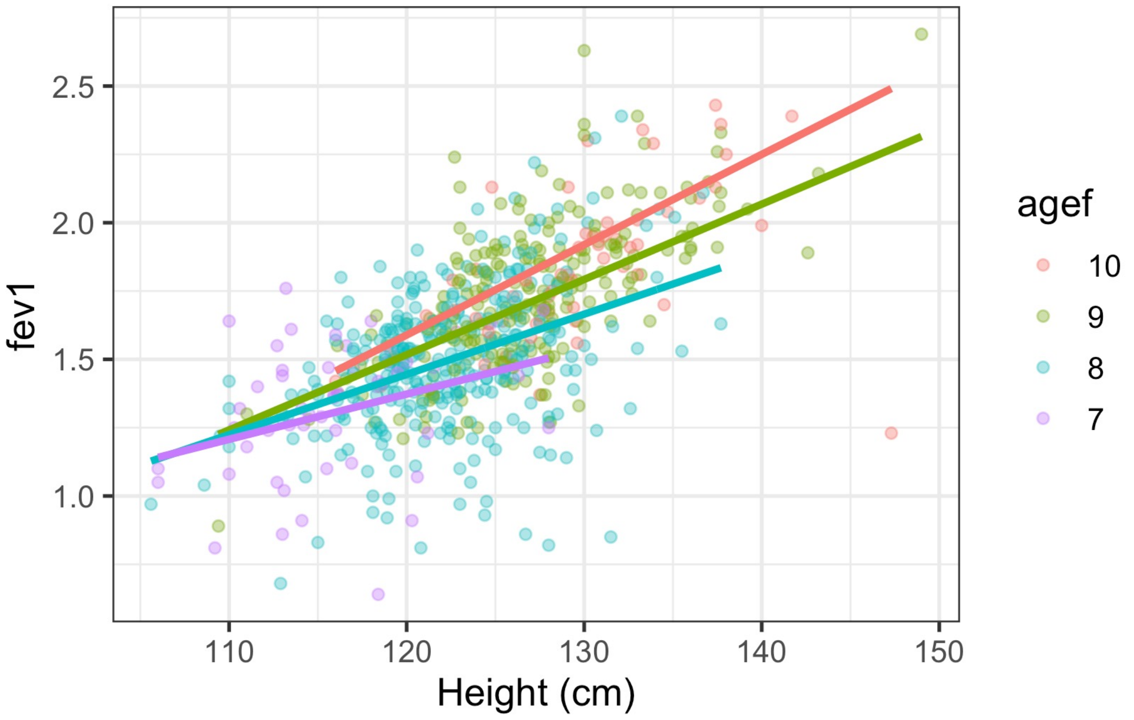
Multiple regression (no interaction)

```
> lm(fev1 ~ age + height, data = peru)
             Estimate Std. Error t value Pr(>|t|)
(Intercept) -2.308601   0.181175 -12.742  < 2e-16 ***
age          0.089714   0.015717   5.708 1.76e-08 ***
height       0.024967   0.001813  13.774  < 2e-16 ***
```



With age x height interaction

```
> lm(fev1 ~ age * height, data = peru)
             Estimate Std. Error t value Pr(>|t|)
(Intercept)  3.793279   1.956125   1.939  0.05292 .
age         -0.587443   0.216724  -2.711  0.00690 **
height      -0.024679   0.015950  -1.547  0.12230
age:height   0.005497   0.001755   3.133  0.00181 **
```



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Transformations

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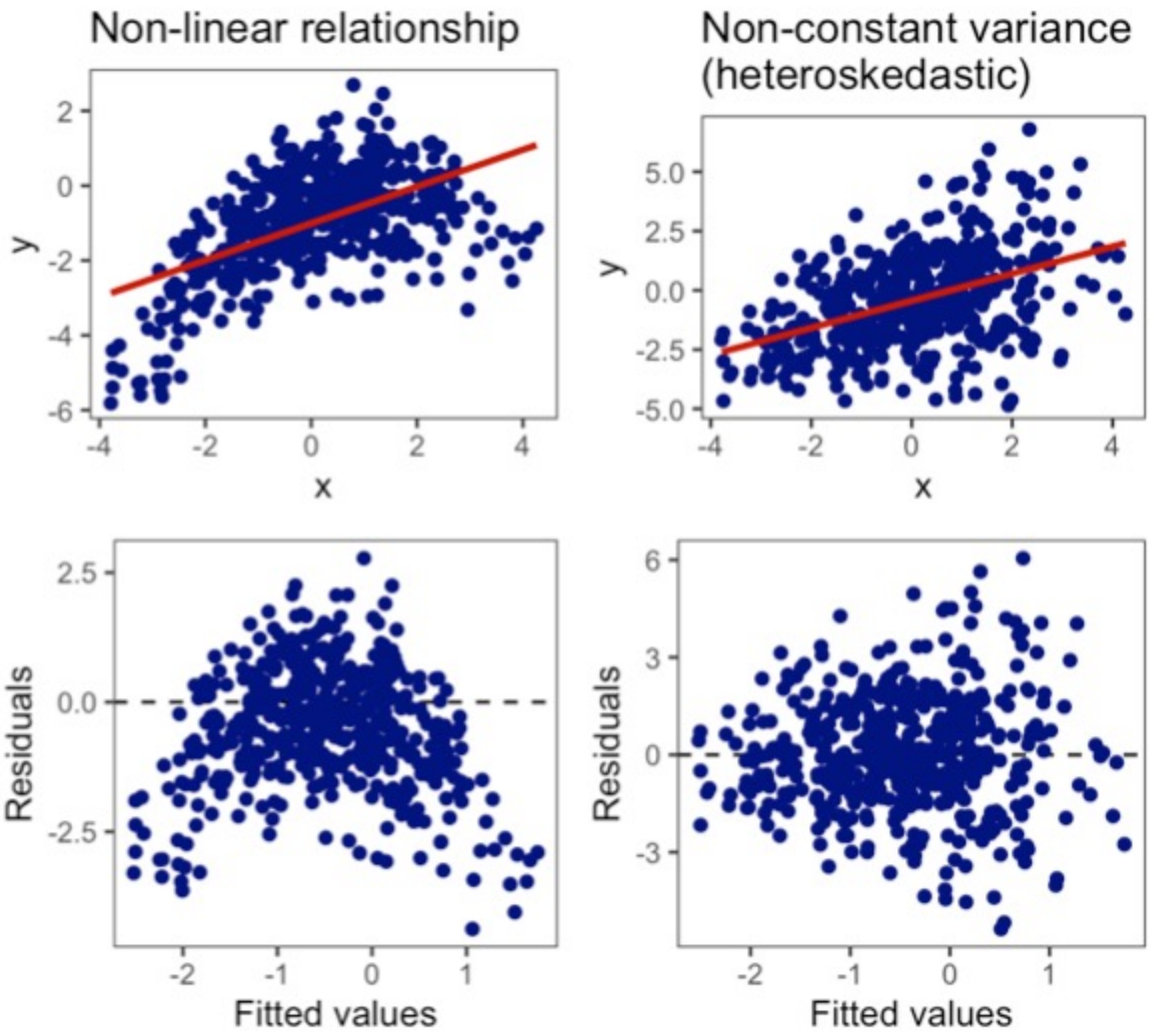
Linear regression assumptions

1. Linearity
2. Normality
3. Independence
4. Equal variance



Strategies for addressing assumption violations

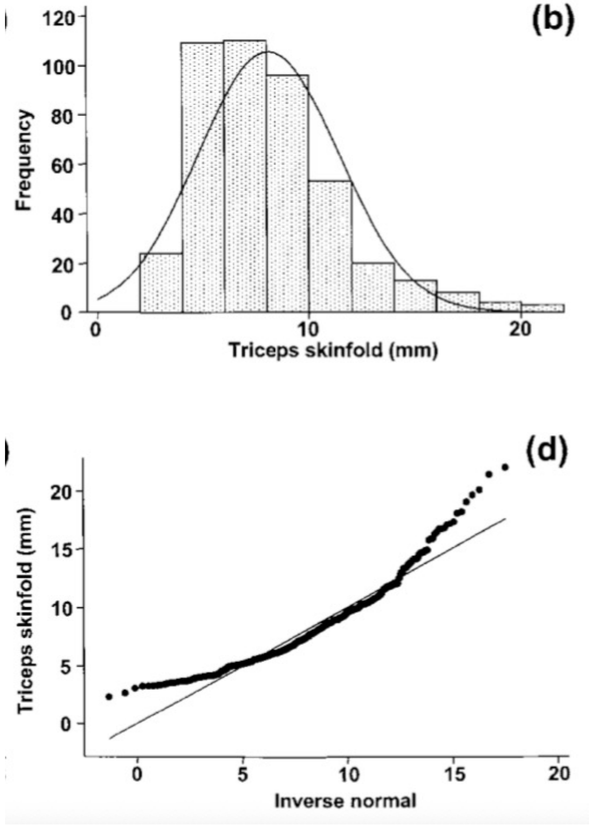
- Check for errors in the data (coding, entry) resulting in outliers.
- Explore non-linear relationships between outcome and exposure variables.
  - Convert continuous variables to categorical.
  - Add quadratic term. allows us to capture curved r/s
- Conduct **sensitivity analysis** to check whether Text excluding outliers / alternative specifications change the key conclusions of the analysis.
- **Use transformations** of outcome or exposure variables.

rnorm() ?

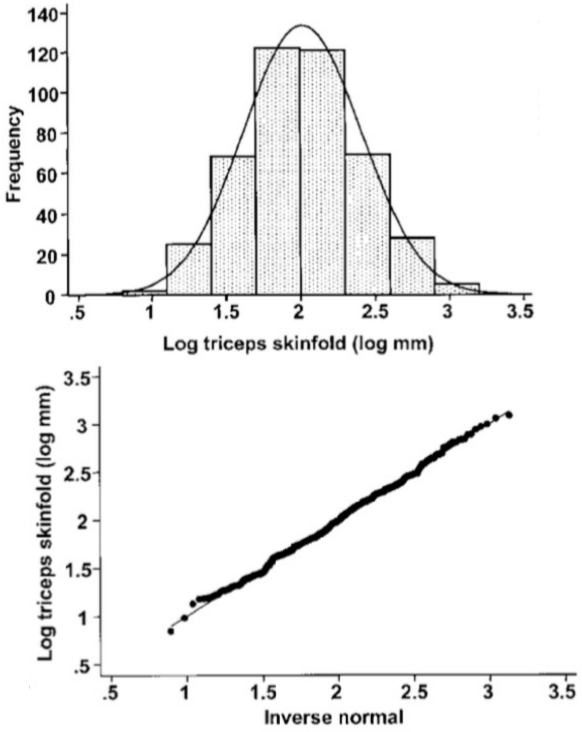
- Use robust standard errors or bootstrapping to derive CIs without requiring distributional assumptions (Chapter 30; Problem Set 3).

Log transformation

- Positively (right) skewed data: Triceps skinfold measurements of 440 men

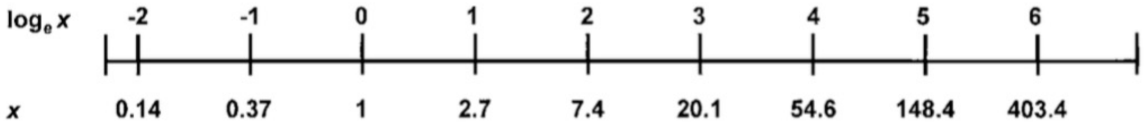


- Log transformation triceps skinfold measurement



Convenient properties:

- Log(y) ~ Normal() → y ~ Log-normal()
- $\log(y) = \beta_0 + \beta_1 x$ → $y = e^{\beta_0} e^{\beta_1 x}$
- "1 unit increase in x → e^{β_1} **<u>times</u>** increase in y"



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Non-linear relationship

log functions as useful

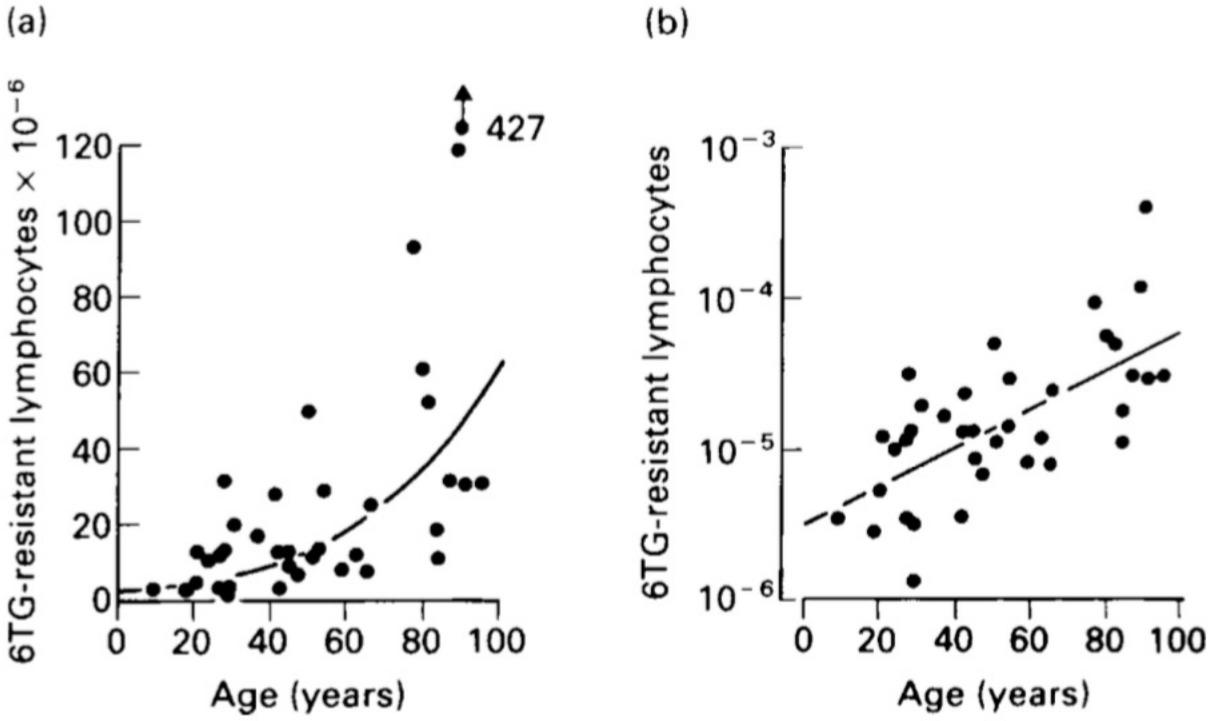

Fig. 13.4 Relationship between frequency of 6TG-resistant lymphocytes and age for 37 individuals drawn using (a) a linear scale, and (b) a logarithmic scale for frequency. Reprinted from Morley *et al*. *Mechanisms of Ageing and Development* **19**: 21–6, copyright (1982), with permission from Elsevier Science.

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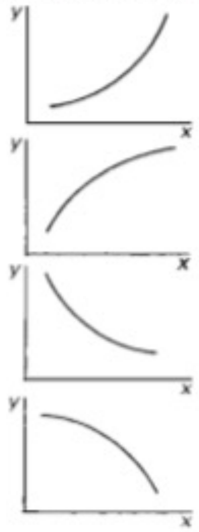
Transformations: summary

- **Unequal variance:** variance increasing with mean is very common situation
  - Diagnose with residuals vs. fitted values—funnel shape.
  - Try logarithmic transformation of outcome variable (S.D. increases linearly with mean).
  - Reciprocal or square-root transformation for more/less severe.

- **Non-linear relationship:**
  - Diagnose with residual vs. fitted values—'U-shaped' pattern.
  - May be resolved by transforming either outcome or exposure variable (see Table 13.3)
  - Often becomes difficult to interpret: "a 1 unit increase in reciprocal of soda intake is associated with a 0.2 unit reduction in square-root of BMI"

- Goodness-of-fit tests (Shapiro-Wilk, chi-squared) tend to be not that useful for data sets of moderate size.
  - Very sensitive to detect some difference from Normal distribution; unclear practical importance for inference.

Table 13.3 Summary of different choices of transformations. Those removing positive skewness are called group A transformations, and those removing negative skewness group B.

Situation	Transformation
Positively skewed distribution (group A)	
Lognormal	Logarithmic ($u = \log x$)
More skewed than lognormal	Reciprocal ($u = 1/x$)
Less skewed than lognormal	Square root ($u = \sqrt{x}$)
Negatively skewed distribution (group B)	
Moderately skewed	Square ($u = x^2$)
More skewed	Cubic ($u = x^3$)
Unequal variation	
s.d. proportional to mean	Logarithmic ($u = \log x$)
s.d. proportional to mean^2	Reciprocal ($u = 1/x$)
s.d. proportional to $\sqrt{\text{mean}}$	Square root ($u = \sqrt{x}$)
Non-linear relationship	Transform: y variable and/or x variable
	Group A (y) Group B (x) Group B (y) Group A (x) Group A (y) Group A (x) Group B (y) Group B (x)

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Model building

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What to include in my regression?

1. Any variables that are *confounders* of the relationship between the outcome and primary exposure of interest.

2. For linear regression (only): other variables that are clearly associated with the outcome → improves precision
   - But keep the number relatively small: interpretation becomes harder with large number of variables.
   - Rule of thumb, at least 10 observations per additional covariate. (Often much more for large or noisy data sets.)

like p val

- For hypothesis testing (e.g. RCTs): full analysis plan must be specified before you start.
- For observational studies (exploratory analysis): some model building required, but write down clear hypotheses and analysis plan before you start.
  - Usually involves **sensitivity analysis**: testing interactions, non-linear terms

- Avoid model selection procedures that involve choosing covariates based on looking at the data:
  - to avoid: Including all covariates with univariate associations; e.g. $p < 0.05$, $p < 0.2$
  - to avoid: 'Stepwise selection': recursively adding / remove variables until no further improvement in model fit

Why should we avoid stepwise models

- Over-optimistic results:
  - P-values for the selected variables tend to be small, CIs narrow and R2 high
  - Higher chance of spurious associations with increasing number of initial variables

- Regression coefficients tend to be larger and as a result perform poorly in test data

- Slight changes in data can lead to large in the variables selected in the final model

- Stepwise methods often used instead of expert knowledge and correct problem definition

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Dangers of collinearity

- Collinearity: high correlation between two exposure variables.

reduces ability to identify main exposure of interest as it is being mocked up by the other covariate

- Not possible to identify linearly independent association with each variable.
  - Only a linear combination of the covariates → biased coefficient estimates
- Can cause very large standard errors; spurious null association with the outcome

fake

Table 29.11 Demonstration of the effect of collinearity, using data from the study of lung disease in children in Lima, Peru. Variable *newage* is variable *age* plus a random error whose standard deviation is given in the first column in the table.

s.d. of random error	Correlation between *age* and *newage*	Regression of height on *newage*	Regression of height on *age* and *newage*		
		Coefficient (s.e.) for *newage*	Coefficient (s.e.) for *age*	Coefficient (s.e.) for *newage*	Sum of coefficients
1	0.57	1.61 (0.20)	5.31 (0.33)	− 0.17 (0.20)	5.16
0.1	0.9904	5.06 (0.28)	6.81 (2.00)	− 1.66 (1.99)	5.15
0.01	0.9999	5.16 (0.28)	21.76 (19.94)	−16.62 (19.94)	5.14

Common pitfalls

Common pitfalls in (Kirkwood & Sterne, section 38.8)

1. **Multiple comparisons:**
   - Even if there is no association between exposure and outcome, 1 in 20 comparisons to be statistically significant at 5% level.
   - Try to minimize the number of hypothesis tests; if testing many, adjust for it.

2. **Subgroup analyses:**
   - Be very cautious about interpreting apparent associations in subgroups of data, particularly when no evidence of overall association.
   - Tempting to emphasise an ‘interesting’ finding in an otherwise null study!

3. **Data-driven comparisons:**
   - Avoid choosing definitions for specifying exposure or outcome variable after running several analyses

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Any questions?