











Kiesha Prem

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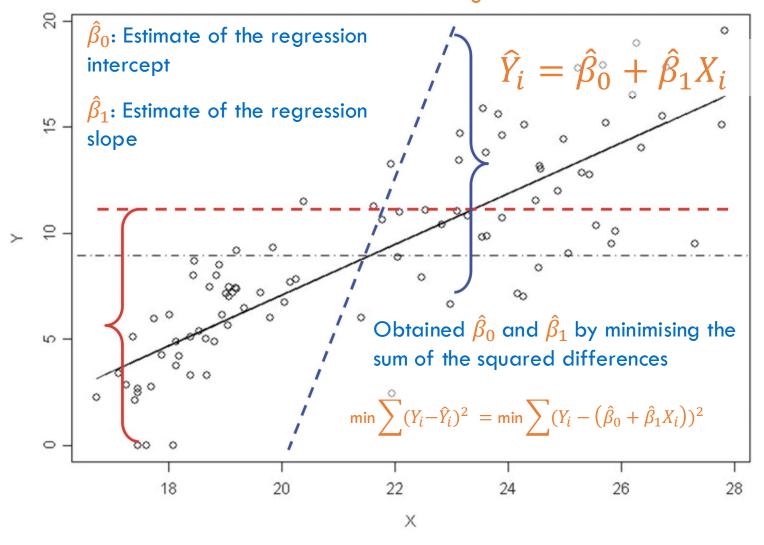
Dependent variable $Y_i = \beta_0 + \beta_1 X_i + \mathcal{E}_i \quad \text{Random error}$ Intercept Slope (regression) coefficient

Minimising error

The equation provides an estimate of the population regression line.



Least Squares Method

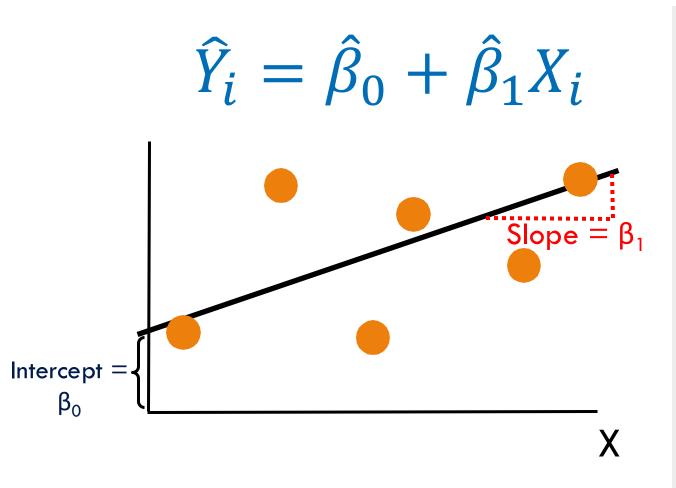




Recap

Interpreting regression coefficients





 β_0 least-square estimate of the regression intercept

- estimated mean value of Y when x = 0
- $\hat{\beta}_1$ least-square estimate of the regression slope
- estimated change in y when x changes by one unit



Inference about the slope



T-test

Null hypothesis

$$H_0$$
: $\hat{\beta}_1 = 0$

no linear relationship

Alternative hypothesis

$$H_1: \hat{\beta}_1 \neq 0$$

linear relationship may exist

Test

$$t = \frac{\left(\widehat{\beta}_1 - 0\right)}{SE\left(\widehat{\beta}_1\right)}$$

with t distribution of d.f. = n - 2

Hypothesis tests

or confidence intervals

- To test the significance or "contribution" of an independent variable (X) to the dependent variable (Y)
- Is there a linear relationship between X and Y?

We are testing for zero slope: If $\hat{\beta}_1 = 0$: then the X does not influence the value of Y

Determining the fit of the model



- We need to determine how well y is predicted by $\widehat{y}(x_i) = \widehat{\beta_0} + \widehat{\beta_1}x_i$
- How much variability in y can be accounted for by the linear regression where x is the predictor?
- The R² indicates the proportion of the total variation explained by the model.
 - If x and y are independent (i.e., no relationship), then $R^2 = 0$.
 - If x and y are perfectly correlated (i.e., perfect relationship), then $R^2 = 1$.
- Hence, R² indicates how well the model is doing in explaining the response and ranges from 0 to 1.

```
> m_ldl_age = lm(chp$ldl ~ chp$age)
> summary(m_ldl_age)
Call:
lm(formula = chp$ldl ~ chp$age)
Residuals:
     Min
               10 Median
-0.13569 -0.10771 -0.08370 -0.05917 0.34480
Coefficients:
              Estimate Std. Error t value
(Intercept) -1.5666710 0.0167344 -93.62 <0.00000000000000002
chp$age
             0.0714981 0.0002448 292.05 < 0.00000000000000002
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 0.1714 on 9998 degrees of freedom
Multiple R-squared: 0.8951, Adjusted R-squared: 0.8951
F-statistic: 8.529e+04 on 1 and 9998 DF, p-value: < 0.00000000000000022
```

$$R^2 = 1 - \frac{SSE}{SST}$$

R-Squared & F-test

Determining the fit of the model



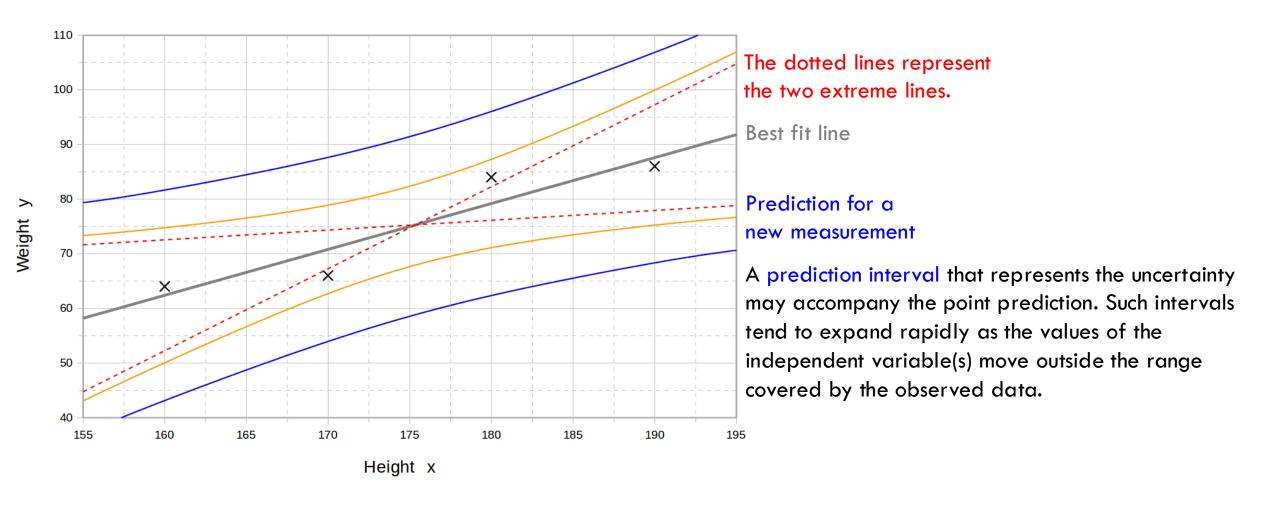
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```

Age explains 89.5% of the variation in LDL cholesterol. From the F-statistic, the p-value is <0.001, indicating the regression model with age is significantly better than a model with intercept term only.

Confidence interval of mean outcome





Confidence interval and prediction interval



The 95% CI of the slope

$$\widehat{\beta_1} \pm t_{n-2,0.025} \operatorname{SE}(\widehat{\beta_1})$$

The 95% CI of the intercept

$$\widehat{\beta_0} \pm t_{n-2,0.025} \operatorname{SE}(\widehat{\beta_0})$$

The 95% CI for the predicted value at a specific x-value, x

$$\hat{y} \pm t_{n-2.0.025} SE(\hat{y})$$

where

$$SE(\hat{y}) = s \sqrt{\frac{1}{n} + \frac{(x - \bar{x})^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2}} \text{ and } s = \sqrt{\frac{\sum_{i=1}^{n} (y_i - \widehat{y_i})^2}{n - 2}}$$

The 95% prediction interval for a predicted value \hat{y} at a specific x-value, x $\hat{y} \pm t_{n-2,0.025}$ $\text{SE}_{pred}(\hat{y})$

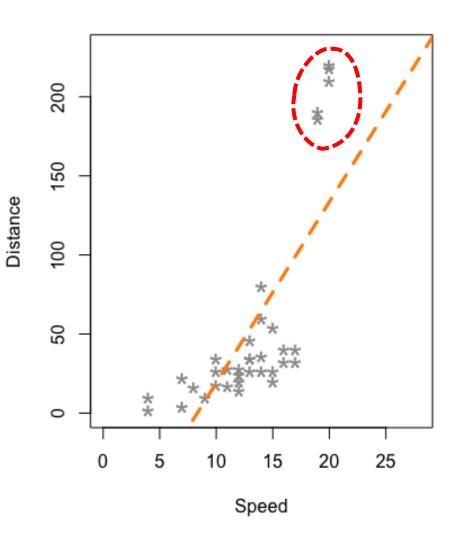
where

$$SE_{pred}(\hat{y}) = s \sqrt{1 + \frac{1}{n} + \frac{(x - \bar{x})^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2}}$$

Reflecting both the uncertainty in the mean response and the natural variability of the data.



With Outliers



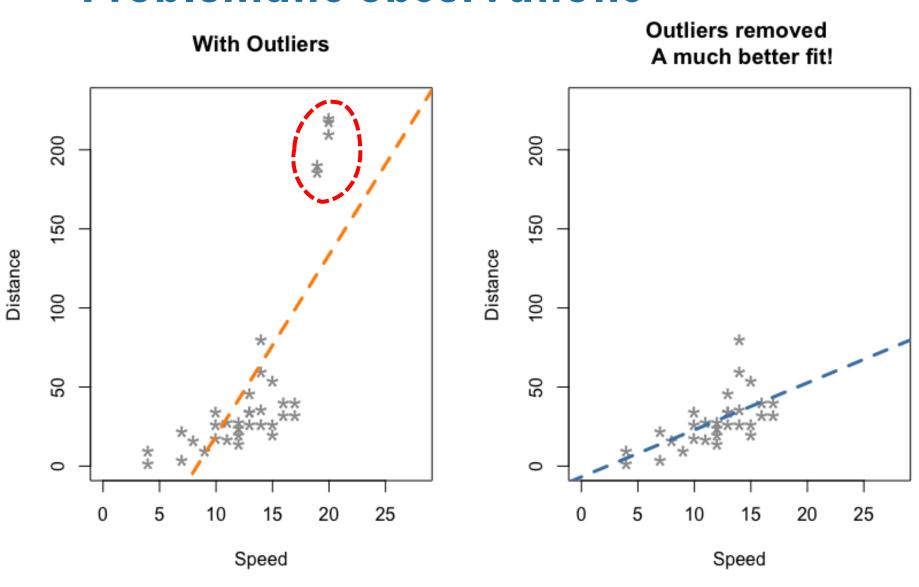
Ideally, each observation should have the same influence on the regression analysis.

If an observation has a significantly greater influence than the rest, it can potentially bias the results.

Some potential characteristics of an influential observation:

- it has a large absolute residual and
- it is far from mean x.

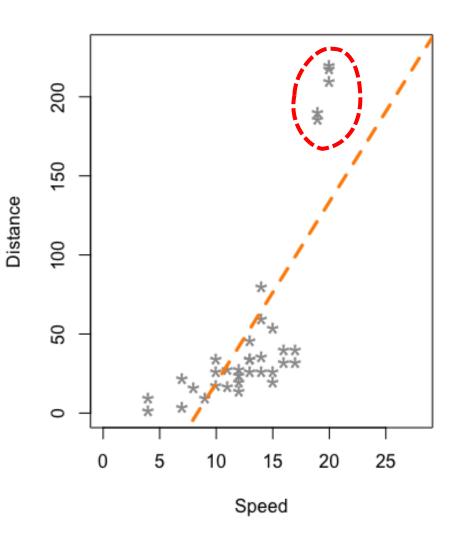




The intercept and slope are different



With Outliers



Leverage is used to quantity the potential of a predictor value influencing the results.

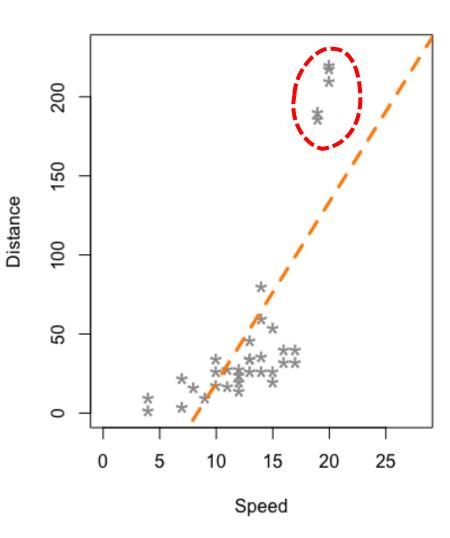
The leverage ranges from 1/n to 1.

The leverage is lowest when the observation is close to the mean of the predictor.

Observation with high leverage is influential if the associated residual is large.



With Outliers



Outlier: An outlier is defined as an observation that has a large residual (i.e., absolute studentised or standardised residual exceeds 2 or 3), hence there is a large discrepancy between the observed outcome and predicted outcome from the linear regression model.

Leverage observations: A leverage observation is defined as an observation with a value of x far away from the mean of x (i.e., exceeding 2 or 3 times the

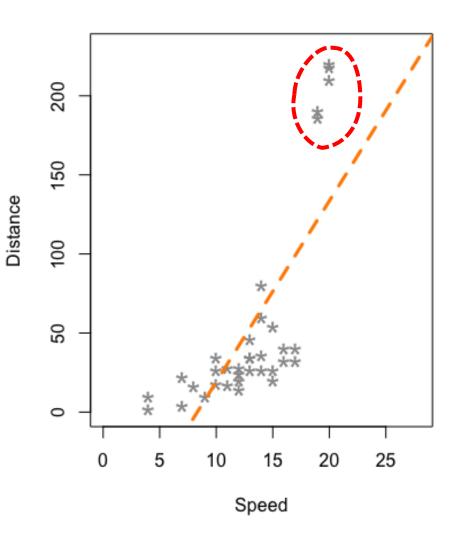
Influential observations: An influential observation is defined as an observation that changes the estimates, and it usually has large residual and high leverage.

average leverage).

Influence statistics



With Outliers



Cook's Distance: A measure that combines the information of leverage and residual of the observation.

Measure	Value
Check the Cook's distance	> 4/n or >1
Check if leverage observation	$>$ 2 \times mean of leverage or $>$ 3 \times mean of leverage
Studentised residual	> 2 or >3

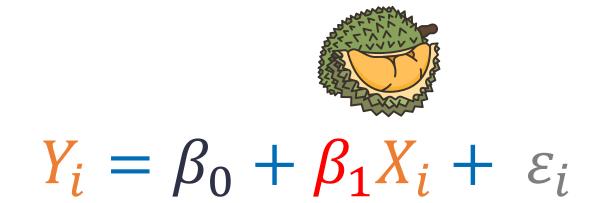




Dependent variable
$$Y_i = \beta_0 + \beta_1 X_i + \mathcal{E}_i \quad \text{Random error}$$
 Intercept Slope (regression) coefficient

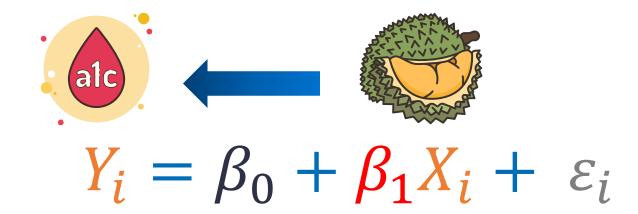








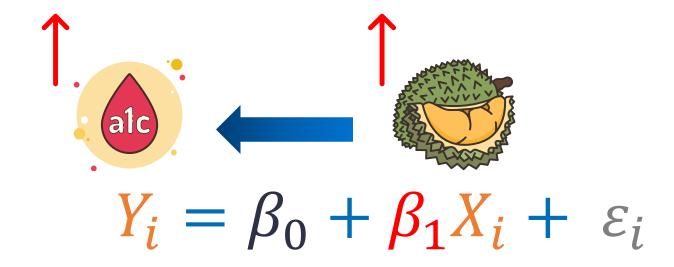






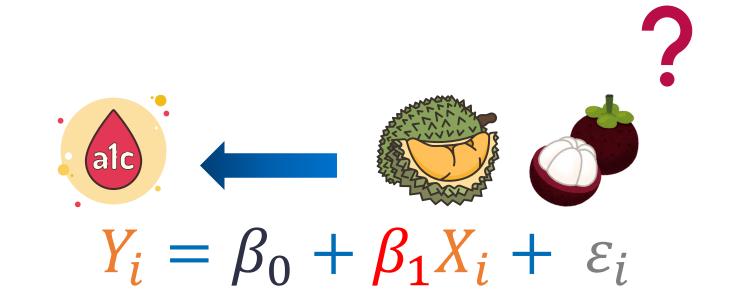
Recap









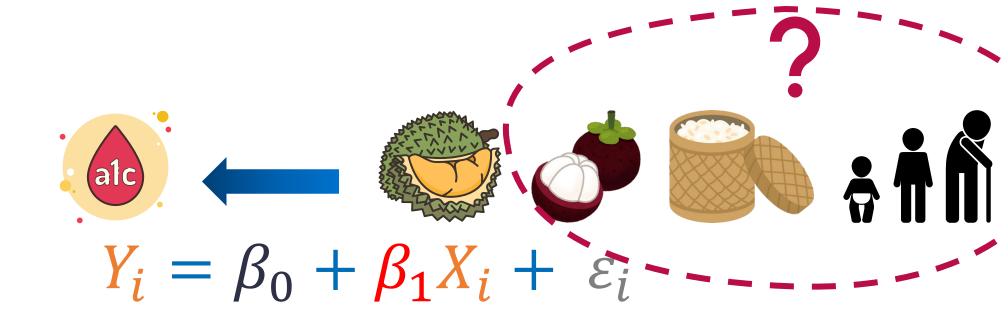














Dependent

Independent variables

variable

$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \dots + \beta_p X_{i,p} + \varepsilon_i$$

Random error



Dependent

Independent variables



$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \dots + \beta_p X_{i,p} + \varepsilon_i$$









Random error



Dependent variable

Independent variables

$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \dots + \beta_p X_{i,p} + \varepsilon_i$$

Intercept

Regression coefficients

Random error

Estimate the relationships between a dependent variable and independent variables



Dependent variable

Independent variables

$$Y_i = \beta_0 + \beta_0 X_{i,1} + \beta_0 X_{i,2} + \cdots + \beta_0 X_{i,p} + \varepsilon_i$$
Intercept

Regression coefficients

Random error

Estimate the relationships between a dependent variable and independent variables



Multiple linear regression can improve our ability to predict an outcome when we have several predictors.

Controlling for confounding when investigating the relationship between the outcome Y_i and a predictor of interest $X_{i,1}$:

- \triangleright A confounding variable (or confounder) is of little immediate interest but is correlated with $X_{i,1}$ and is independently related to the outcome.
- $\triangleright \beta_1$ is the effect of $X_{i,1}$ on yi among subjects with the same values of $X_{i,2}$, $X_{i,3}$, ..., $X_{i,p}$.
- > The predictor of interest sometimes called the exposure.

How do you interpret the beta values?



Multiple linear regression can improve our ability to predict an outcome when we have several predictors.

Controlling for confounding when investigating the relationship between the

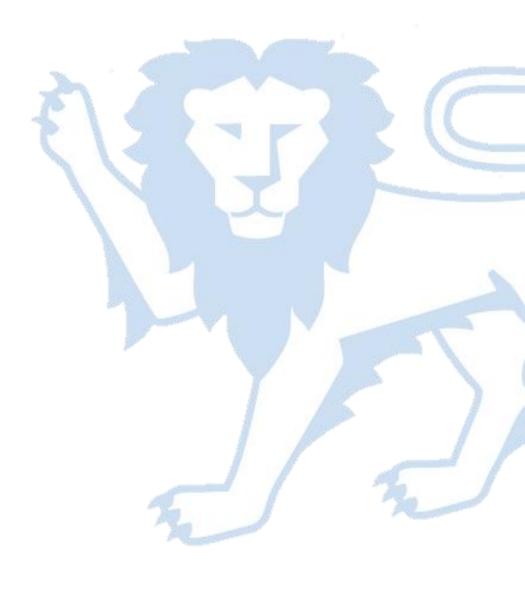
- outcome Y_i and a predictor of interest $X_{i,1}$:
 - \triangleright A confounding variable (or confounder) is of little immediate interest but is correlated with X_i^{op} and is independently related to the outcome.
 - $\nearrow \beta_1$ is the effect of $X_{i,2}$ on yi among subjects with the same values of $X_{i,2}$, X_i , X_i , X_i
 - The predictor of interest sometimes called the exposure

How do you interpret the beta values?





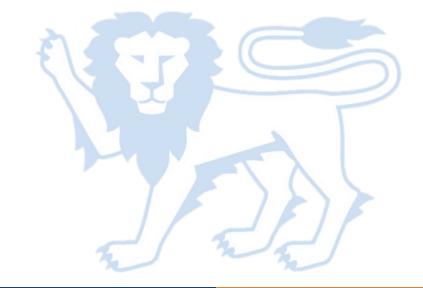
An example: factors associated with cardiovascular risk



Construct a multiple linear regression model



```
Call:
lm(formula = cvdData$ldl ~ cvdData$bmi + cvdData$age + factor(cvdData$race) +
    cvdData$gender)
Residuals:
    Min
            10 Median
                                   Max
-2.1799 -0.5896 -0.0071 0.5171 2.0219
Coefficients:
                            Estimate Std. Error t value Pr(>|t|)
                                                  4.789 3.57e-06 ***
(Intercept)
                            2.463024
                                       0.514288
cvdData$bmi
                            0.043112
                                       0.017408
                                                  2.477 0.01422 *
cvdData$age
                            0.013287
                                       0.006313
                                                  2.105 0.03676 *
factor(cvdData$race)Chinese -0.100631
                                                -0.643
                                       0.156395
                                                        0.52078
factor(cvdData$race)Malays
                            0.188735
                                       0.157285
                                                  1.200
                                                        0.23179
cvdData$genderFemale
                           -0.430744
                                       0.128996 -3.339 0.00103 **
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 0.8535 on 174 degrees of freedom
Multiple R-squared: 0.1172, Adjusted R-squared: 0.09185
F-statistic: 4.621 on 5 and 174 DF, p-value: 0.0005523
```



95% confidence intervals of the parameters



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Call:
lm(formula = cvdData$ldl ~ cvdData$bmi + cvdData$age + factor(cvdData$race) +
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<pre>> confint(m1)</pre>		
	2.5 %	97.5 %
(Intercept)	1.4479788565	3.47806887
cvdData\$bmi	0.0087547782	0.07746964
cvdData\$age	0.0008266835	0.02574644
<pre>factor(cvdData\$race)Chinese</pre>	-0.4093052309	0.20804383
<pre>factor(cvdData\$race)Malays</pre>	-0.1216975597	0.49916669
cvdData\$genderFemale	-0.6853428156	-0.17614555

How do you interpret these results?



95% confidence intervals of the parameters



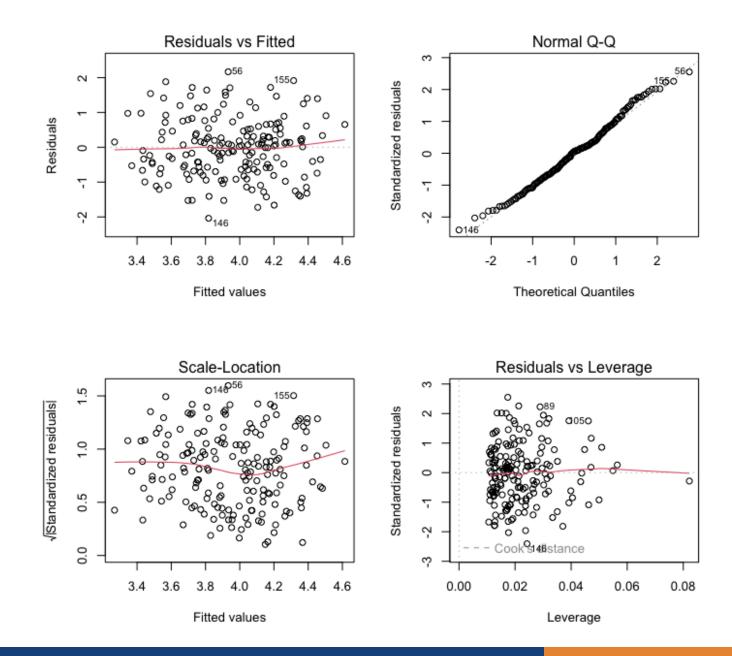
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                                           0.49916669
cvdData$genderFemale
                            -0.6853428156 -0.17614555
```

How do you interpret these results?

The effect of the age on LDL cholesterol is 0.0133 (95%Cl: 0.0008–0.02575, p=0.0368) when the age increases by 1 year with an adjustment for BMI, race and sex.

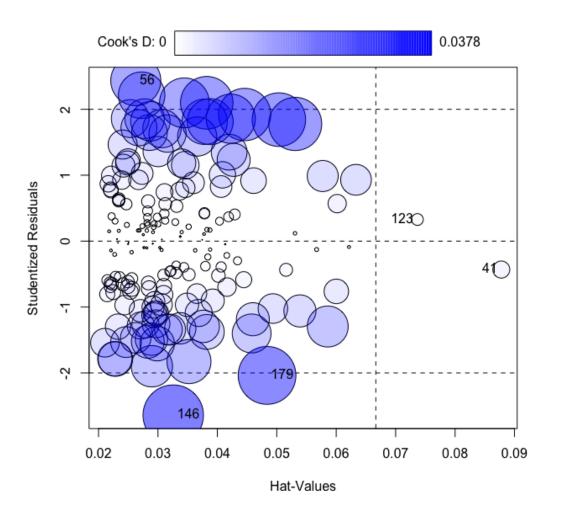
Model diagnostics



Influential plot



Studentised residual vs leverage with Cook's distance



The observations listed are the top 2 largest absolute residuals (i.e., 56 and 146) or hat values (i.e., 41 and 123) or Cook's distances (i.e., 146 and 179). Let us remove these observations (i.e., 41st, 56th, 123th, 146th and 179th observations) and re-run the multiple linear regression analysis to compare the difference in the estimates.

Remove potentially influential observations

Call:



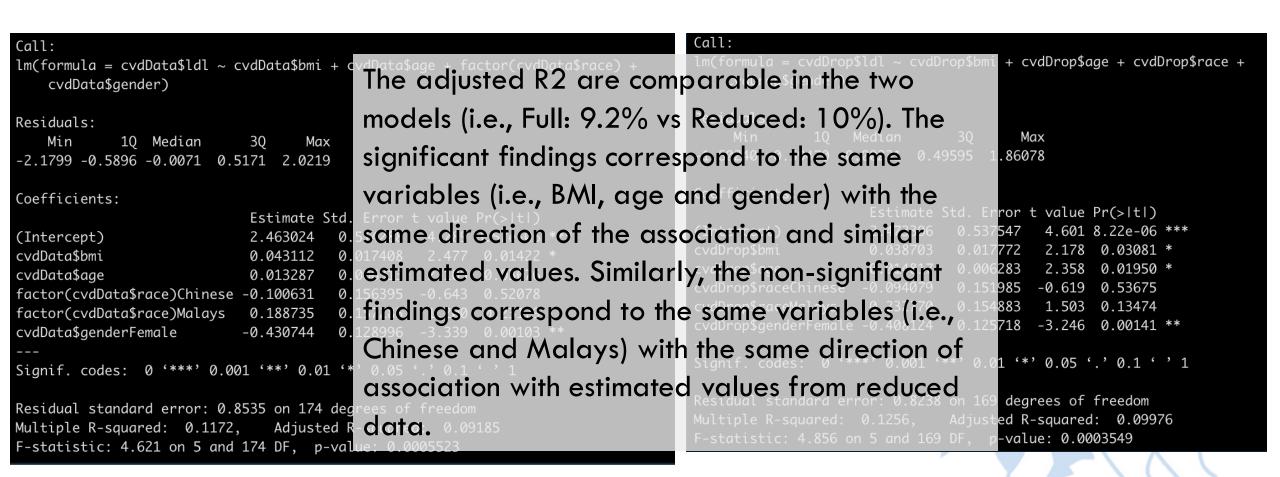
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```
lm(formula = cvdDrop$ldl ~ cvdDrop$bmi + cvdDrop$age + cvdDrop$race +
    cvdDrop$gender)
Residuals:
               10 Median
                                        Max
     Min
-1.60240 -0.59470 -0.00231 0.49595 1.86078
Coefficients:
                     Estimate Std. Error t value Pr(>|t|)
(Intercept)
                     2.473306
                                0.537547 4.601 8.22e-06 ***
cvdDrop$bmi
                     0.038703
                                0.017772
                                           2.178 0.03081 *
                                0.006283
                                                 0.01950 *
cvdDrop$age
                     0.014817
                                           2.358
cvdDrop$raceChinese -0.094079
                                0.151985
                                         -0.619
                                                 0.53675
cvdDrop$raceMalays
                     0.232770
                                0.154883
                                           1.503 0.13474
cvdDrop$genderFemale -0.408124
                                0.125718 -3.246 0.00141 **
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 0.8238 on 169 degrees of freedom
Multiple R-squared: 0.1256,
                               Adjusted R-squared: 0.09976
F-statistic: 4.856 on 5 and 169 DF, p-value: 0.0003549
```

How do you interpret these results?

Remove potentially influential observations





How do you interpret these results?





Dependent variable

Independent variables

$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \dots + \beta_p X_{i,p} + \varepsilon_i$$

Intercept

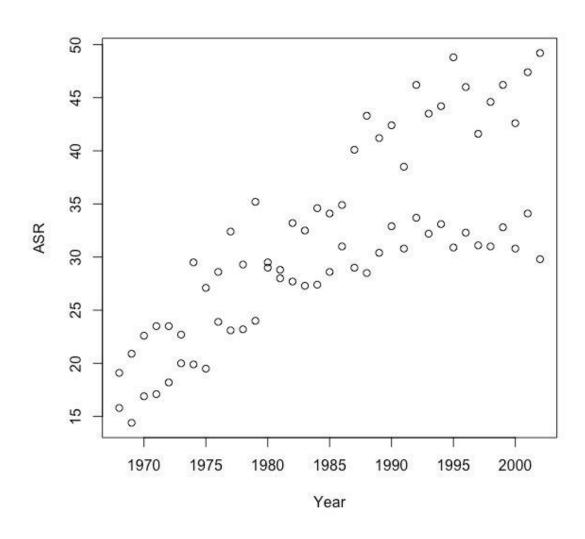
Regression coefficients

Random error

Estimate the relationships between a dependent variable and independent variables

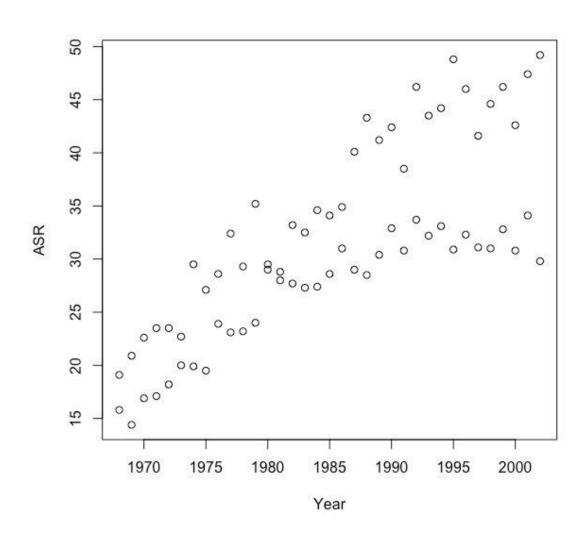
Colorectal cancer incidence in Singapore



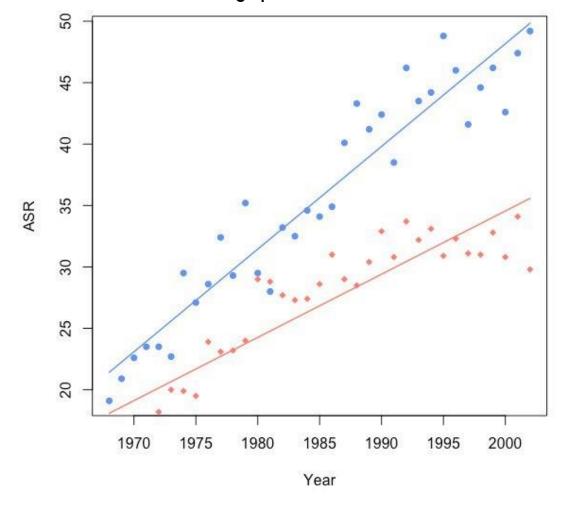


Colorectal cancer incidence in Singapore





The linear temporal trend of rates from 1968 to 2002 is different between Singapore Chinese males and females.



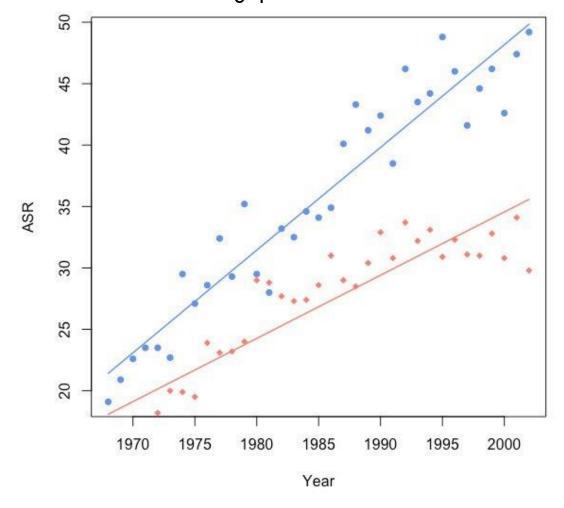
Modelling interaction

- In most scientific questions, for example, is smoking prevalence associated with cancer incidence rate?
- The answer is simple: Yes
- However, some answers to a scientific question can be complex: It depends.

Interaction (or effect modification) occurs when the magnitude of the effect of the exposure variable on an outcome (i.e., the association) differs depending on the level of a third variable (i.e. effect modifier).



The linear temporal trend of rates from 1968 to 2002 is different between Singapore Chinese males and females.

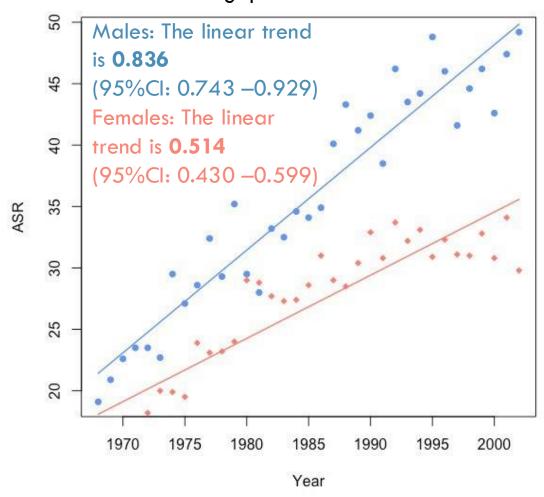


Modelling interaction: fit separate models?



```
summary(m_male)
Call:
lm(formula = both$ASR[both$Female %in% 0] ~ both$Year[both$Female %in%
   ([0
                                                                   Stratified
Residuals:
   Min
            10 Median
                                                                   analysis
-5.5643 -1.5821 -0.4786 1.7071 5.1643
Coefficients:
                                Estimate Std. Error t value
                                                                       Pr(>|t|)
(Intercept)
                             -1623.26429
                                           90.53351 -17.93 <0.000000000000000000
both$Year[both$Female %in% 0]
                                 0.83571
                                            0.04561
                                                      18.32 < 0.00000000000000000 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
Residual standard error: 2.725 on 33 degrees of freedom
Multiple R-squared: 0.9105,
                              Adjusted R-squared: 0.9078
F-statistic: 335.8 on 1 and 33 DF, p-value: < 0.000000000000000022
> summary(m_female)
Call:
lm(formula = both$ASR[both$Female %in% 1] ~ both$Year[both$Female %in%
   1])
Residuals:
    Min
            10 Median
-5.7805 -1.9270 0.1223 1.5716 4.7381
Coefficients:
                              Estimate Std. Error t value
                                                                   Pr(>|t|)
(Intercept)
                             -994.4121
                                                  -12.01 0.0000000000001355
both$Year[both$Female %in% 1]
                               0.5145
                                           0.0417
                                                   12.34 0.0000000000000657 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' ' 1
Residual standard error: 2.492 on 33 degrees of freedom
Multiple R-squared: 0.8218, Adjusted R-squared: 0.8164
 -statistic: 152.2 on 1 and 33 DF, p-value: 0.00000000000006573
```

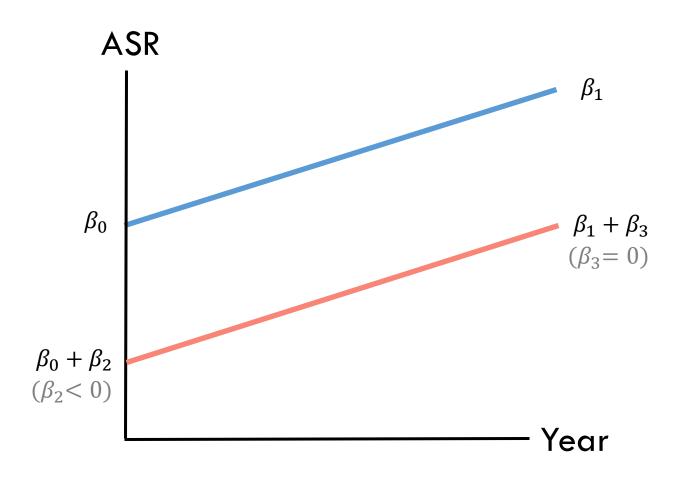
The linear temporal trend of rates from 1968 to 2002 is different between Singapore Chinese males and females.



Interpretation of model with interaction



$$ASR_i = \beta_0 + \beta_1 Year_i + \beta_2 Female_i + \beta_3 (Year_i \times Female_i) + \varepsilon_i$$



T-test

Null hypothesis

$$H_0: \beta_3 = 0$$

Alternative hypothesis

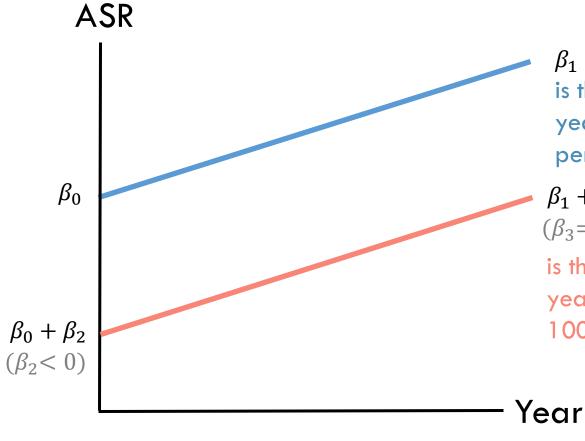
$$H_1: \beta_3 \neq 0$$

Interpretation of model with interaction



$$ASR_i = \beta_0 + \beta_1 Year_i + \beta_2 Female_i + \beta_3 (Year_i \times Female_i) + \varepsilon_i$$

$$ASR_i = (\beta_0 + \beta_2 Female_i) + (\beta_1 + \beta_3 Female_i) Year_i + \varepsilon_i$$



is the linear trend for males, i.e., as $Year_i$ changes by 1 year, ASR_i is expected to change by β_1 per 100,000 person-years

$$\beta_1 + \beta_3$$
$$(\beta_3 = 0)$$

is the linear trend for males, i.e., as Year_i changes by 1 year, ASR_i is expected to change by $(\beta_1 + \beta_3)$ per 100,000 person-years

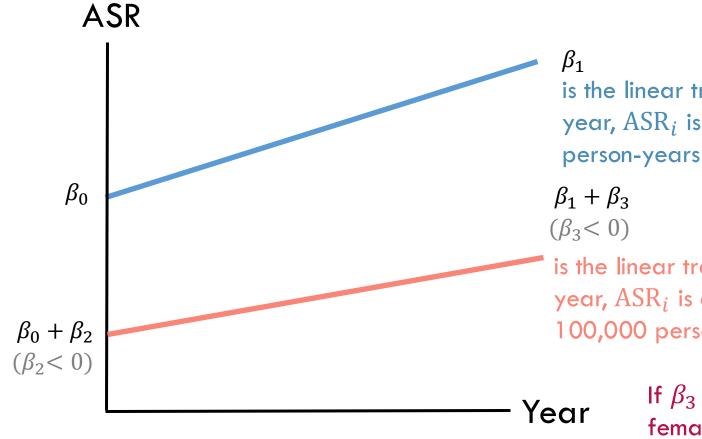
> If $\beta_3 = 0$ the linear trend between males and females is the same, i.e., parallel lines.

Interpretation of model with interaction



$$ASR_i = \beta_0 + \beta_1 Year_i + \beta_2 Female_i + \beta_3 (Year_i \times Female_i) + \varepsilon_i$$

$$ASR_i = (\beta_0 + \beta_2 Female_i) + (\beta_1 + \beta_3 Female_i) Year_i + \varepsilon_i$$



is the linear trend for males, i.e., as $Year_i$ changes by 1 year, ASR_i is expected to change by β_1 per 100,000 person-years

is the linear trend for males, i.e., as $Year_i$ changes by 1 year, ASR_i is expected to change by $(\beta_1+\beta_3)$ per 100,000 person-years

If $\beta_3 \neq 0$ the linear trend between males and females is the different, i.e., non-parallel lines.

Modelling interaction: Intercept



```
Call:
lm(formula = both$ASR ~ both$Year.centered * both$Female.factor)
Residuals:
            10 Median
   Min
                                  Max
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                                         Estimate Std. Error t value
                                                                               Pr(>|t|)
(Intercept)
                                          35.6286
                                                      0.4413 80.731 < 0.00000000000000000 ***
both$Year.centered
                                           0.8357
                                                             19.125 < 0.000000000000000000
both$Female.factorFemale
                                          -8.7943
                                                      both$Year.centered:both$Female.factorFemale -0.3212
                                                     0.0618 -5.198
                                                                             0.00000212 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142,
                              Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.00000000000000022
```

We centre the mean year to improve the interpretation of the intercept.

Recall, the linear model for males:

$$ASR_i = \beta_0 + \beta_1 \mathbf{Year}_i + \varepsilon_i$$

With mean centred year:

$$ASR_i = \beta_0 + \beta_1 (Year_i - 1985) + \varepsilon_i$$

The intercept β_0 is the mean ASR among males at 1985, which is 35.6 per 100,000 person-years.

Modelling interaction: Interaction



```
Call:
lm(formula = both$ASR ~ both$Year.centered * both$Female.factor)
Residuals:
            10 Median
   Min
                                  Max
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                                         Estimate Std. Error t value
                                                                               Pr(>|t|)
(Intercept)
                                                     0.4413 80.731 < 0.000000000000000002
both$Year.centered
                                                            19.125 < 0.000000000000000000
both$Female.factorFemale
                                          -8.7943
                                                     both$Year.centered:both$Female.factorFemale -0.3212
                                                     0.0618 -5.198
                                                                             0.00000212 **
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 '' 1
Residual standard error: 2.611 on 66 degrees of freedom
                             Adjusted R-squared: 0.9103
Multiple R-squared: 0.9142,
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.00000000000000022
```

The interaction factor of two predictors, $Year_i$ and $Female_i$, is a multiplication of the two predictors.

Linear trend for males: β_1 $\widehat{\beta_1} = 0.836$

Linear trend for females: $\beta_1 + \beta_3$ $\widehat{\beta_1} + \widehat{\beta_3} = 0.836 + (-0.321) = 0.515$

The linear trend between males and females is **significantly different** (p-value<0.001).

Modelling interaction: How do we decide?



	How do we decide whether to include an interaction in the model?
	☐ Prior belief about the relationship between two predictors and outcome.
	☐ Exploratory data analysis (e.g., plots and assessing the significance of the interaction term).
2	So, how many predictors should we include in an interaction?
	□ Seldom consider the interaction between 3 or more predictors (i.e., multiplying three or predictors together) because the explanation becomes difficult and can potentially be meaningless.
	☐ Here we will only consider interactions consisting of two predictors (i.e., two-way interactions)

Type I compares the variables sequentially in the model.

Let us consider the model (m1) where the variables are specified as:

Year.centered + Female.factor + Year.centered:Female.factor

Note that mean centred year (Year.centered) was specified first, followed by female (Female.factor), and finally the interaction between the first two variables (Year.centered:Female.factor).

```
> m1 = lm(both$ASR~both$Year.centered + both$Female.factor + both$Year.centered:both$Female.factor)
> summary(m1)
Call:
lm(formula = both$ASR ~ both$Year.centered + both$Female.factor +
    both$Year.centered:both$Female.factor)
Residuals:
             10 Median
    Min
                                    Max
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                                            Estimate Std. Error t value
                                                                                    Pr(>|t|)
(Intercept)
                                                         0.4413 \quad 80.731 < 0.000000000000000000
                                             35.6286
both$Year.centered
                                             0.8357
                                                                19.125 < 0.000000000000000000
both$Female.factorFemale
                                             -8.7943
                                                         0.6241 - 14.091 < 0.000000000000000000
both$Year.centered:both$Female.factorFemale -0.3212
                                                         0.0618 -5.198
                                                                                  0.00000212 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' '1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142, Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.000000000000000022
> anova(m1)
Analysis of Variance Table
Response: both$ASR
                                     Df Sum Sa Mean Sa F value
both$Year.centered
                                      1 3254.1 3254.1 477.367 < 0.0000000000000000022
both$Female.factor
                                       1 1353.4 1353.4 198.545 < 0.0000000000000000022
both$Year.centered:both$Female.factor 1 184.2 184.2 27.021
                                                   6.8
Residuals
                                      66 449.9
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '. '0.1 ' '1
```

Type I would provide the variation explained by:

- Mean centred year with the model having mean centred year only (giving p-value for slope of mean centred year)
- Female with the model having mean centred year and female only(giving p-value for slope of value for slope of female after adjusting for mean centred year)
- Interaction with the model having mean centred year, female, and interaction (giving p-value for slope of interaction after adjusting for mean centred year and female)

```
m1 = lm(both$ASR~both$Year.centered + both$Female.factor + both$Year.centered:both$Female.factor)
> summary(m1)
Call:
lm(formula = both$ASR ~ both$Year.centered + both$Female.factor +
    both$Year.centered:both$Female.factor)
Residuals:
             10 Median
    Min
                                    Max
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                                            Estimate Std. Error t value
                                                                                   Pr(>|t|)
                                                                80.731 < 0.000000000000000000
(Intercept)
                                            35.6286
both$Year.centered
                                             0.8357
                                                                19.125 < 0.000000000000000000
both$Female.factorFemale
                                            -8.7943
                                                         0.6241 - 14.091 < 0.000000000000000000
both$Year.centered:both$Female.factorFemale -0.3212
                                                        0.0618 -5.198
                                                                                  0.00000212 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' '1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142, Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.000000000000000022
> anova(m1)
Analysis of Variance Table
Response: both$ASR
                                     Df Sum Sa Mean Sa F value
both$Year.centered
                                      1 3254.1 3254.1 477.367 < 0.0000000000000000022
both$Female.factor
                                      1 1353.4 1353.4 198.545 < 0.0000000000000000022
both$Year.centered:both$Female.factor 1 184.2 184.2 27.021
Residuals
                                                   6.8
                                     66 449.9
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '. '0.1 ' '1
```

Now let us consider the model (m2) where the variables are specified as:

Year.centered:Female.factor + Female.factor + Year.centered

Note that interaction was specified first, followed by female, and finally mean centred year.

```
m2 = lm(both$ASR~both$Year.centered.Female + both$Female.factor + both$Year.centered)
 summary(m2)
Call:
lm(formula = both$ASR ~ both$Year.centered.Female + both$Female.factor +
    both$Year.centered)
Residuals:
             10 Median
   Min
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                          Estimate Std. Error t value
                                                                  Pr(>|t|)
(Intercept)
                           35.6286
                                       0.4413 \quad 80.731 < 0.000000000000000002
both$Year.centered.Female -0.3212
                                      0.0618 -5.198
both$Female.factorFemale
                          -8.7943
                                      0.6241 - 14.091 < 0.000000000000000000
both$Year.centered
                            0.8357
                                      0.0437 19.125 < 0.000000000000000002
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142,
                               Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.000000000000000022
 anova(m2)
Analysis of Variance Table
Response: both$ASR
                          Df Sum Sa Mean Sa F value
                                                                    Pr(>F)
both$Year.centered.Female 1 944.95 944.95 138.62 < 0.000000000000000022
both$Female.factor
                           1 1353.44 1353.44 198.55 < 0.000000000000000022
both$Year.centered
                          1 2493.35 2493.35 365.77 < 0.000000000000000022
Residuals
                          66 449.91
                                       6.82
               0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Type I would provide the variation explained by:

- Interaction with the model having the interaction only (giving p-value for slope of interaction)
- Female with the model having interaction and female only(giving pvalue for slope of value for slope of female after adjusting for interaction)
- Mean centred year with the model model having interaction, female and mean centred year (giving p-value for slope of mean centred year after adjusting for interaction and female)

Order matters!

```
m2 = lm(both$ASR~both$Year.centered.Female + both$Female.factor + both$Year.centered)
 summary(m2)
Call:
lm(formula = both$ASR ~ both$Year.centered.Female + both$Female.factor +
    both$Year.centered)
Residuals:
   Min
             10 Median
                                    Max
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                          Estimate Std. Error t value
                                                                  Pr(>|t|)
(Intercept)
                           35.6286
                                              80.731 < 0.000000000000000002
both$Year.centered.Female -0.3212
                                       0.0618 -5.198
both$Female.factorFemale
                           -8.7943
                                       0.6241 - 14.091 < 0.0000000000000000002
both$Year.centered
                            0.8357
                                       0.0437 19.125 < 0.000000000000000002
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142,
                               Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.00000000000000022
> anova(m2)
Analysis of Variance Table
Response: both$ASR
                          Df Sum Sa Mean Sa F value
both$Year.centered.Female 1
                             944.95 944.95 138.62 < 0.000000000000000022
both$Female.factor
                           1 1353.44 1353.44 198.55 < 0.000000000000000022
both$Year.centered
                           1 2493.35 2493.35 365.77 < 0.000000000000000022
Residuals
                          66 449.91
                                        6.82
                0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1_' ' 1
```



```
m1 = lm(both$ASR~both$Year.centered + both$Female.factor + both$Year.centered:both$Female.factor)
> summary(m1)
Call:
lm(formula = both$ASR ~ both$Year.centered + both$Female.factor +
   both$Year.centered:both$Female.factor)
Residuals:
   Min
            10 Median
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                                         Estimate Std. Error t value
                                                                               Pr(>|t|)
(Intercept)
                                          35.6286
                                                      0.4413 80.731 < 0.00000000000000000 ***
both$Year.centered
                                           0.8357
                                                      0.0437 19.125 < 0.00000000000000000 ***
both$Female.factorFemale
                                          -8.7943
                                                      0.0618 -5.198
both$Year.centered:both$Female.factorFemale -0.3212
                                                                             0.00000212 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142, Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.000000000000000022
```

```
> m2 = lm(both$ASR~both$Year.centered.Female + both$Female.factor + both$Year.centered)
> summary(m2)
Call:
lm(formula = both$ASR ~ both$Year.centered.Female + both$Female.factor +
    both$Year.centered)
Residuals:
    Min
             10 Median
-5.7805 -1.8196 -0.1932 1.6035 5.1643
Coefficients:
                          Estimate Std. Error t value
                                                                  Pr(>ltl)
(Intercept)
                           35.6286
                                       0.4413 \quad 80.731 < 0.000000000000000002
both$Year.centered.Female -0.3212
                                      0.0618 -5.198
both$Female.factorFemale -8.7943
                                       0.6241 - 14.091 < 0.00000000000000000
both$Year.centered
                            0.8357
                                       0.0437 19.125 < 0.00000000000000000 ***
Sianif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 2.611 on 66 degrees of freedom
Multiple R-squared: 0.9142, Adjusted R-squared: 0.9103
F-statistic: 234.3 on 3 and 66 DF, p-value: < 0.000000000000000022
```

The two models gave the same estimates for the predictors and the same R².



The Type I of m1 and m2 gave different sum of squares (i.e., Sum Sq) and p-values (esp. interaction).

Order is important for Type I

Collinearity



Predictors are naturally correlated.

Collinearity is a problem when adding correlated predictors into the model, resulting in a very large increase in the standard errors of some estimates.

The collinearity problem entangles the effects of predictors and complicates the interpretation.

Collinearity



Collinearity occurs when two or more predictors have a linear relationship (or are highly correlated).

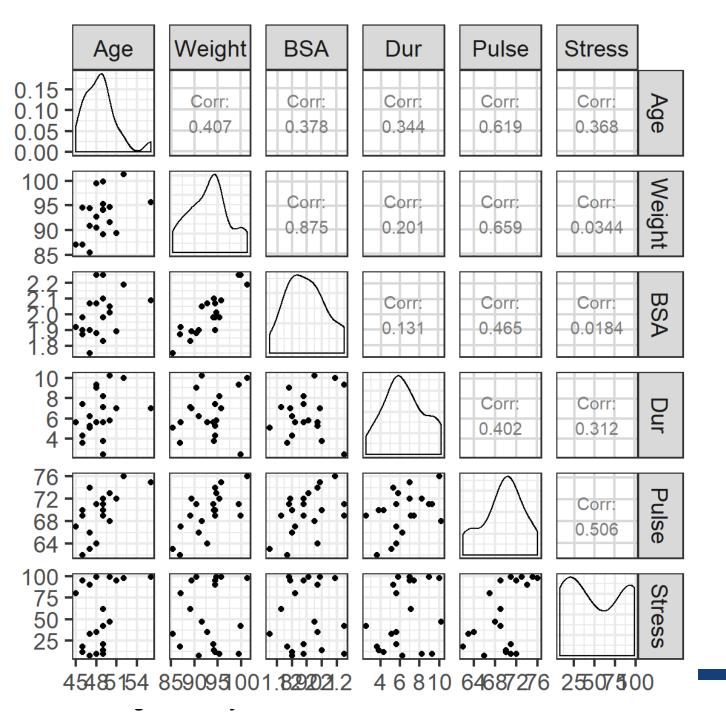
Among current smokers, these three variables:

- (i) age at survey,
- (ii) age started smoking, and
- (iii) duration of smoking (in years), are related in a linear expression:

Age at survey = Age started smoking + Smoking duration

Estimates for these predictors are not uniquely estimated because of the exact linear expression (i.e., perfect collinearity).

Software may drop one of the predictors when there is perfect collinearity (e.g., the correlation between predictors is 1).



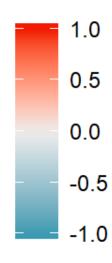


Pairwise scatterplot



Heat map of correlation coefficients





Variance inflation factor (VIF)



Quantifies how much the variance of the estimate (or standard error) is **inflated** because of the **collinearities among the predictors** (when compared with no collinearity)

- a) VIF of 1 for the jth predictor means no correlation between this predictor and the remaining predictors in the model (i.e., no inflation in variance).
- b) VIF > 4 warrants further investigation.
- c) VIF > 10 is a sign of serious collinearity requiring correction.

Big VIF is bad → means inflated (high) uncertainty in estimates

- Remove problematic (highly correlated) variables
- ☐ Use linearly combine the predictor variables

Variance inflation factor (VIF)



VIF is not applicable to categorical variables with three or more groups.

A generalised variance inflation factor (GVIF) was proposed with degrees of freedom (df) of a categorical variable corresponding to:

df = number of groups -1

The **GVIF**^{1/(2 x df)} is reported, and it reduces to the square root of VIF when the variable is continuous or binary, suggesting:

- \triangleright a GVIF^{1/(2 x df)} > 2 = sqrt(4) warrant further investigation.
- ightharpoonup a GVIF^{1/(2 x df)} > 3.2 \approx sqrt(10) is a sign of serious collinearity requiring correction.

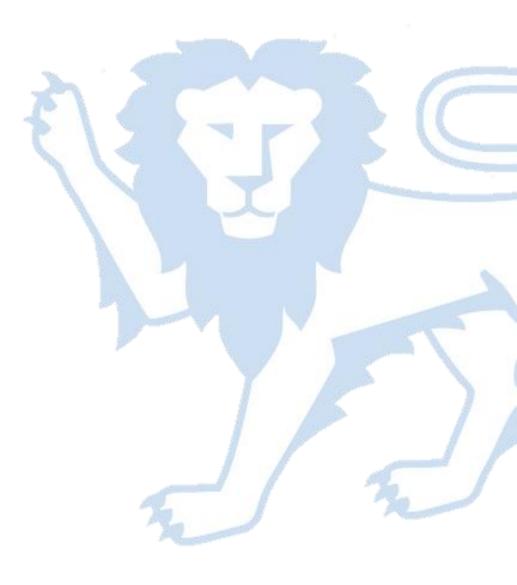


"Choose well. Your choice is brief, and yet endless."

— Johann Wolfgang von Goethe



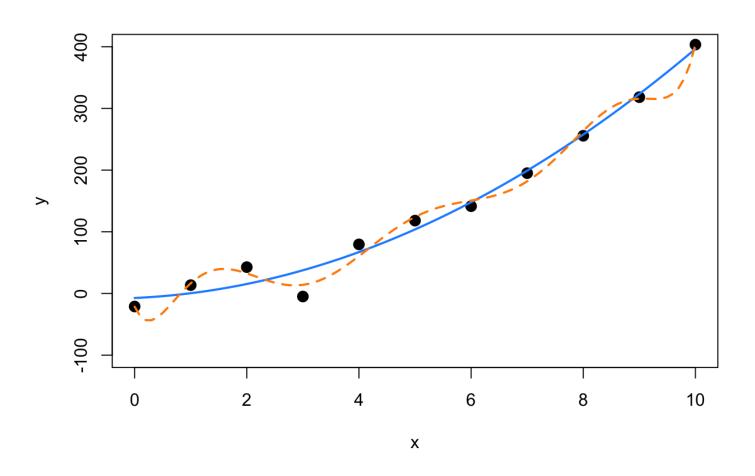
In linear regression





Which is better? orange line vs blue line

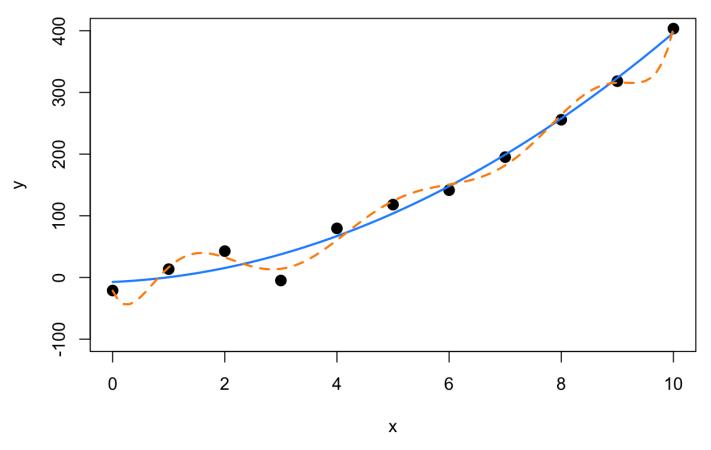






Which is better? orange line vs blue line





Are you overfitting your model?



Why do we need to choose well?



Trade-offs between goodness-of-fit and model complexity

Use variable selection procedures to find a good model from a set of possible models (e.g., no collinearity issues)

Understand the two uses of models:

- 1. explanation
- 2. prediction

How can we choose well?



- 1.Stepwise (+ backward and forward) variable selection Easy to implement in R
- 2. Variable selection criterion:
- compare the models AIC, C_p and BIC
- Smaller AIC and BIC indicate better model fit

Multiple linear regression



Dependent

Independent variables

variable

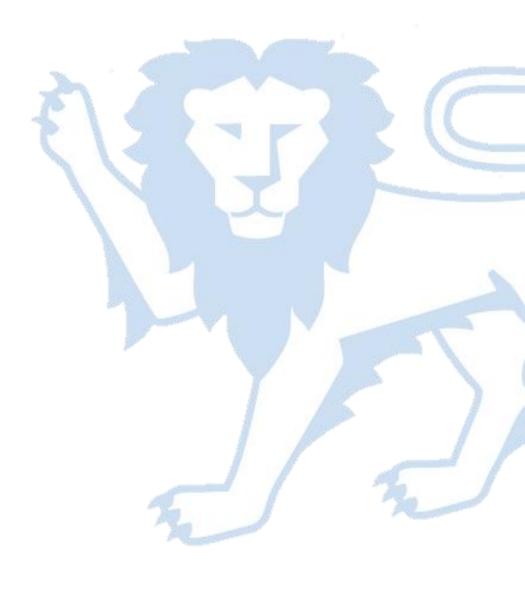
$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \dots + \beta_p X_{i,p} + \varepsilon_i$$

Random error





An example: factors associated with cardiovascular risk



Task 0: Construct a multiple linear regression model



```
> # Task 0: Construct a multiple linear regression model
> mod = lm(tcData$chol ~ tcData$age+ tcData$bmi.1+ tcData$bmi.2+ tcData$gender+ tcData$smoker)
> # Task 1: Interpret the model output
> summary(mod)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.1 + tcData$bmi.2 +
   tcData$gender + tcData$smoker)
Residuals:
   Min
           10 Median
                               Max
-3.5015 -0.6799
                     0.6644 3.5606
              0.0074
Coefficients:
                       Estimate Std. Error t value
                                                         Pr(>|t|)
                                 (Intercept)
                       1.878677
tcData$age
                                 0.042216
tcData$bmi.1
                       0.010177
                                 0.040052
                                          0.254
                                                           0.7994
tcData$bmi.2
                       0.052434
                                 0.040058
                                          1.309
                                                           0.1906
tcData$gendermale
                       0.008556
                                 0.028249
                                          0.303
                                                           0.7620
tcData$smokerex smoker
                      -0.010881
                                 0.035801
                                         -0.304
                                                           0.7612
tcData$smokernever smoker -0.081607
                                 0.032791 -2.489
                                                           0.0129 *
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
Residual standard error: 1.02 on 5206 degrees of freedom
Multiple R-squared: 0.1935,
                           Adjusted R-squared: 0.1926
F-statistic: 208.2 on 6 and 5206 DF, p-value: < 0.00000000000000022
```

Fit a multiple linear regression model with chol as the outcome and the following variables as the predictors: age, bmi.1, bmi.2, gender, and smoker.

Task 1: Interpret the model output

```
Saw Swee Hock School of Public Health
```

```
> # Task 0: Construct a multiple linear regression model
> mod = lm(tcData$chol ~ tcData$age+ tcData$bmi.1+ tcData$bmi.2+ tcData$gender+ tcData$smoker)
> # Task 1: Interpret the model output
> summary(mod)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.1 + tcData$bmi.2 +
   tcData$gender + tcData$smoker)
Residuals:
   Min
           10 Median
                               Max
-3.5015 -0.6799
              0.0074 0.6644 3.5606
Coefficients:
                       Estimate Std. Error t value
                                                         Pr(>|t|)
                                 (Intercept)
                       1.878677
tcData$age
                       0.042216
                                 tcData$bmi.1
                       0.010177
                                0.040052
                                          0.254
                                                           0.7994
tcData$bmi.2
                       0.052434
                                0.040058
                                         1.309
                                                          0.1906
tcData$gendermale
                       0.008556
                                0.028249
                                          0.303
                                                          0.7620
tcData$smokerex smoker
                                                          0.7612
                      -0.010881
                                0.035801
                                         -0.304
tcData$smokernever smoker -0.081607
                                0.032791 -2.489
                                                          0.0129 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 1.02 on 5206 degrees of freedom
Multiple R-squared: 0.1935,
                           Adjusted R-squared: 0.1926
F-statistic: 208.2 on 6 and 5206 DF, p-value: < 0.00000000000000022
```

Based on the model you have fitted in Task 1, report and interpret the effect of body mass index on total cholesterol.

Task 1: Interpret the model output

```
> # Task 0: Construct a multiple linear regression model
> mod = lm(tcData$chol ~ tcData$age+ tcData$bmi.1+ tcData$bmi.2+ tcData$gender+ tcData$smoker)
> # Task 1: Interpret the model output
> summary(mod)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.1 + tcData$bmi.2 +
   tcData$gender + tcData$smoker)
Residuals:
   Min
           10 Median
-3.5015 -0.6799
                     0.6644 3.5606
              0.0074
Coefficients:
                       Estimate Std. Error t value
                                                          Pr(>|t|)
(Intercept)
                       1.878677
                                 tcData$age
                                 0.042216
                                 0.040052
tcData$bmi.1
                       0.010177
                                           0.254
                                                           0.7994
tcData$bmi.2
                       0.052434
                                                           0.1906
                                 0.040058
                                           1.309
tcData$gendermale
                       0.008556 - 0.028249 - 0.303
                                                           Ø.7620
tcData$smokerex smoker
                       -0.010881
                                 0.035801
                                                           0.7612
                                          -0.304
tcData$smokernever smoker -0.081607
                                 0.032791
                                         -2.489
                                                           0.0129 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 1.02 on 5206 degrees of freedom
Multiple R-squared: 0.1935,
                            Adjusted R-squared: 0.1926
F-statistic: 208.2 on 6 and 5206 DF, p-value: < 0.00000000000000022
```



A one kg/m2 increase in BMI would increase the mean total cholesterol by 0.010 mmol/l and 0.052 mmol/l for the first and second measurement of BMI, respectively, after adjusting for age, gender and smoking status. Hence, both BMI measurements have a positive association with total cholesterol.

However, their p-values are greater than 0.05. As such, the effect of BMI measured before and after physical examination are non-significant, suggesting BMI and total cholesterol are not associated after adjusting for age, gender and smoking status.



Generate the variance inflation factors for the model built. Report the variable(s) with a collinearity problem and the corresponding variance inflation factor(s).

Justify your answer.





```
> vif(mod)
                   GVIF Df GVIF^(1/(2*Df))
tcData$age
               1.000554 1
                                  1.000277
tcData$bmi.1 52.108078
                                  7.218593
tcData$bmi.2 52.107294 1
                                  7.218538
tcData$gender 1.000404
                                  1.000202
tcData$smoker 1.000724 2
                                  1.000181
> round(cov2cor(vcov(mod)),3)
                          (Intercept) tcData$age tcData$bmi.1 tcData$bmi.2 tcData$gendermale tcData$smokerex smoker tcData$smokernever smoker
(Intercept)
                                1.000
                                           -0.377
                                                        -0.065
                                                                     -0.061
                                                                                        -0.094
                                                                                                                                          -0.108
                                                                                                               -0.098
tcData$age
                               -0.377
                                           1.000
                                                         0.012
                                                                     -0.011
                                                                                        0.006
                                                                                                                0.017
                                                                                                                                          0.000
tcData$bmi.1
                               -0.065
                                           0.012
                                                         1.000
                                                                     -0.990
                                                                                        -0.010
                                                                                                                0.007
                                                                                                                                          -0.003
tcData$bmi.2
                               -0.061
                                          -0.011
                                                        -0.990
                                                                      1.000
                                                                                        0.008
                                                                                                               -0.008
                                                                                                                                          0.003
tcData$gendermale
                               -0.094
                                           0.006
                                                        -0.010
                                                                      0.008
                                                                                        1.000
                                                                                                               -0.007
                                                                                                                                          -0.012
tcData$smokerex smoker
                               -0.098
                                           0.017
                                                         0.007
                                                                     -0.008
                                                                                        -0.007
                                                                                                                1.000
                                                                                                                                          0.420
tcData$smokernever smoker
                                                                      0.003
                                                                                                                                           1.000
                               -0.108
                                           0.000
                                                        -0.003
                                                                                        -0.012
                                                                                                                0.420
```

Among the predictors, bmi.1 and bmi.2 may have a collinearity problem because their VIFs are 51.108 and 52.107, respectively, and larger than 10.



Fit two multiple linear regression models similar to Task 0 where chol is the outcome and the following variables are still predictors: age, gender and smoker, BUT bmi.1 and bmi.2 are included as predictors in two separate models.

Based on the models you have fitted, compare these findings with those in Task 1.



```
mod1 = lm(tcData$chol ~ tcData$age+ tcData$bmi.1+ tcData$gender+ tcData$smoker)
> summary(mod1)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.1 + tcData$gender +
    tcData$smoker)
Residuals:
   Min
            10 Median
-3.5129 -0.6752 0.0081 0.6625 3.5448
Coefficients:
                          Estimate Std. Error t value
                                                                Pr(>|t|)
(Intercept)
                          1.889766
                                             13.734 < 0.0000000000000000000
                                    0.137600
tcData$age
                          0.042235
                                    0.001262 33.458 < 0.000000000000000000
tcData$bmi.1
                                              0.062099
                                    0.005550
tcData$gendermale
                         0.008254
                                    0.028250
                                               0.292
                                                                  0.7702
tcData$smokerex smoker
                         -0.010491
                                                                  0.7695
                                    0.035802
                                              -0.293
tcData$smokernever smoker -0.081756
                                    0.032793 -2.493
                                                                  0.0127 *
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' '1
Residual standard error: 1.02 on 5207 degrees of freedom
Multiple R-squared: 0.1932,
                              Adjusted R-squared: 0.1925
F-statistic: 249.4 on 5 and 5207 DF, p-value: < 0.00000000000000022
```

BMI and total cholesterol has a positive association as the estimated effects are greater than 0 after adjusting for age, gender and smoking status.





```
> mod2 = lm(tcData$chol ~ tcData$age+ tcData$bmi.2+ tcData$gender+ tcData$smoker)
> summary(mod2)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.2 + tcData$gender +
   tcData$smoker)
Residuals:
            10 Median
   Min
                                  Max
-3.5010 -0.6792 0.0075 0.6644 3.5636
Coefficients:
                         Estimate Std. Error t value
                                                              Pr(>|t|)
                                    0.137551 13.675 < 0.00000000000000000 ***
(Intercept)
                         1.880941
tcData$age
                                    0.042212
tcData$bmi.2
                         0.062515
                                    0.005549
                                            11.265 <0.00000000000000000 ***
tcData$gendermale
                         0.008626
                                    0.028245
                                              0.305
                                                                0.7601
                                    0.035797
tcData$smokerex smoker
                        -0.010946
                                             -0.306
                                                                0.7598
tcData$smokernever smoker -0.081579
                                    0.032787 -2.488
                                                                0.0129 *
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' '1
Residual standard error: 1.019 on 5207 degrees of freedom
Multiple R-squared: 0.1935,
                              Adjusted R-squared: 0.1927
F-statistic: 249.9 on 5 and 5207 DF, p-value: < 0.00000000000000022
```

BMI and total cholesterol has a positive association as the estimated effects are greater than 0 after adjusting for age, gender and smoking status.

0.062 (=0.010+0.052) is close to the adjusted effect of BMI:

- bmi.1 (i.e., 0.062 in mod 1)
- bmi.2 (i.e., 0.063 in mod2).



```
> mod2 = lm(tcData$chol ~ tcData$age+ tcData$bmi.2+ tcData$gender+ tcData$smoker)
> summary(mod2)
Call:
lm(formula = tcData$chol ~ tcData$age + tcData$bmi.2 + tcData$gender +
   tcData$smoker)
Residuals:
           10 Median
   Min
                                Max
-3.5010 -0.6792 0.0075 0.6644 3.5636
Coefficients:
                        Estimate Std. Error t value
                                                           Pr(>|t|)
                                  0.137551 13.675 < 0.00000000000000000 ***
(Intercept)
                        1.880941
tcData$age
                        0.042212
                                  tcData$bmi.2
                        0.062515
                                  tcData$gendermale
                                  0.028245
                        0.008626
                                           0.305
                                                             0.7601
tcData$smokerex smoker
                       -0.010946
                                  0.035797 -0.306
                                                            0.7598
tcData$smokernever smoker -0.081579
                                  0.032787 -2.488
                                                            0.0129 *
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' '1
Residual standard error: 1.019 on 5207 degrees of freedom
Multiple R-squared: 0.1935, Adjusted R-squared: 0.1927
F-statistic: 249.9 on 5 and 5207 DF, p-value: < 0.00000000000000022
```

The SE of the adjusted effects of BMI in Task 1 is much larger than Task 3

Task 1:

0.04005 for bmi.1

0.04006 and bmi.2

VS

Task 3: 0.00555 for both bmi.1 and bmi.2.



Generate the variance inflation factors for the model built in Task 3. Report the variable(s) with a collinearity problem and the corresponding variance inflation factor(s).

Justify your answer





```
> vif(mod1)
                  GVIF Df GVIF^(1/(2*Df))
tcData$age
              1.000423
                                 1.000211
tcData$bmi.1 1.000250
                                  1.000125
tcData$gender 1.000338
                                 1.000169
tcData$smoker 1.000595
                                 1.000149
> vif(mod1)
                  GVIF Df GVIF^(1/(2*Df))
tcData$age
              1.000423
                                 1.000211
tcData$bmi.1 1.000250
                                  1.000125
tcData$gender 1.000338
                                 1.000169
tcData$smoker 1.000595
                                  1.000149
```

In both models, there are no variables with a collinearity problem as their VIF is close to 1 and less than 4 (or 10).

TM-CM02



Biostatistics for Public Health



3 2 assignments







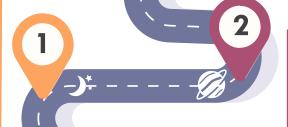


Logistic regression

Data prep, descriptive & inferential statistics, logistics regression and others if we have time









Hypothesis testing



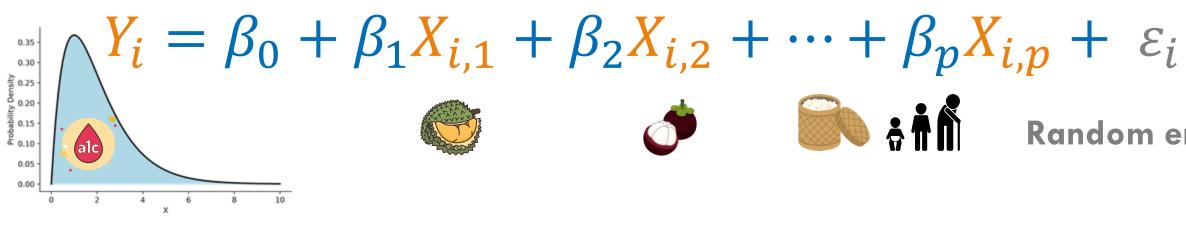
Inferential statistics

Multiple linear regression



Dependent variable

Independent variables







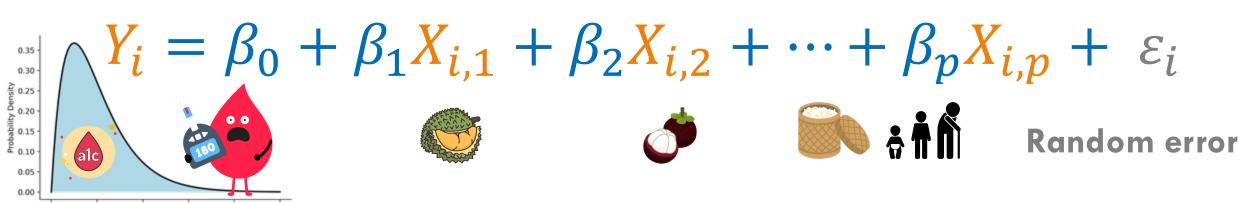


Logistic regression



Dependent variable

Independent variables



Dependent 0: no T2DM

variable 1: T2DM

What type of data? Which model?



Multiple linear regression is suitable for a numerical continuous outcome variable.

- Model: Multiple linear regression
- What is modelled: The mean value of the outcome

Example: To describe the linear relationship between the response variable (weight) and explanatory variables (age and sex).

• The model can be used to determine whether variations in weight could be explained by age and/or sex:

Mean weight =
$$\beta_0 + \beta_1$$
(age) + β_2 (sex)

In more general terms, a linear model is written:

Mean
$$(Y) = \beta_0 + \beta_1 X_1 + \beta_2 X_2$$

• where eta_0 is the intercept and eta_1 and eta_2 are the slopes for variables X_1 and X_2 respectively

What type of data? Which model?



Linear regression

Only appropriate for continuous response variables, which have a Normal distribution at each level of the predictor variable but it is not appropriate for modelling the risk or prevalence of disease, measures which are more common in epidemiology.

We use a different type of statistical model when fitting for risk or prevalence studies. In this model, the log odds of disease are used as the measure of disease outcome.

Binary outcome

Model: Logistic regression

What is modelled: The log of the odds of the outcome

But why do we use log odds?



Thank you