# **Statistical Model Building**

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# How to use this workshop

Workshops developed by the Statistical Consulting Team within the Sydney Informatics Hub form an integrated modular framework. Researchers are encouraged to choose modules to **create custom programmes tailored to their specific needs.** This is achieved through:

- Short 90 minute workshops, acknowledging researchers rarely have time for long multi day workshops.
- Providing statistical workflows appliable in any software, that give practical step by step instructions which researchers return to when analysing and interpreting their data or designing their study e.g. workflows for designing studies for strong causal inference, model diagnostics, interpretation and presentation of results.
- Each one focusing on a specific statistical method while also integrating and referencing the others to give a holistic understanding of how data can be transformed into knowledge from a statistical perspective from hypothesis generation to publication.

For other workshops that fit into this integrated framework refer to our training link page under statistics <u>https://www.sydney.edu.au/research/facilities/sydney-informatics-hub/workshops-and-training.html#stats</u>

# **Research Workflows**

## – So... what is a workflow?

- The process of doing any statistical analysis follows the same general "shape".
- We provide a general research workflow, and a specific workflow for each major step in your research

(currently experimental design, power calculation, analysis using linear models/survival/multivariate/survey methods)

- You will need to tweak them to your needs
- Why do we need a research workflow?
  - As researchers we are motivated to find answers quickly
  - But we need to be systematic in order to
    - Find the right method
    - Use it correctly
    - Interpret and report our results accurately
  - The payoff is huge, we can avoid mistakes that would affect the quality of our work and get to the answers sooner



# Using this workshop after today

These slides should be used after the workshop as reference material and include these workflows for you to follow

- Todays workshop gives you the **statistical workflow**, which is software agnostic in that they can be applied in any software.
- There may also be accompanying software workflows that show you how to do it.
   We won't be going through these in detail. But if you have problems we have a monthly hacky hour where people can help you.

**1on1 assistance** You can request a consultation for more in-depth discussion of the material as it relates to your specific project. Consults can be requested via our Webpage (link is at the end of this presentation)

# **During the workshop**

Ask short questions or clarifications during the workshop. There will be breaks during the workshop for longer questions.



Slides with this blackboard icon are mainly for your reference, and the material will not be discussed during the workshop.



## **Challenge Question**

- A wild boar is coming towards you at 200mph. Do you:?
  - A. Ask it directions
  - B. Wave a red flag
  - C. Wave a white flag
  - D. Begin preparing a trap



# Types of statistical models

## - Any "regression type" model, e.g.

- Linear Model (LM numeric outcome variable)
- Generalised Linear Model (GLM e.g. binary or count outcome variable)
- Linear Mixed Model (LMM LM with a random effect, e.g. repeated measures)
- Generalised Linear Mixed Model (GLMM GLM with random effect)
- Survival analysis (e.g. Cox semi-parametric regression; parametric regression)
- Structural Equation Modelling
- Bayesian Modelling
- Models of spatial data

### Modelling is a very important part of quantitative research work.

# A question for you:

## What is your experience level with regression-type modelling?

- a) No theoretical or practical experience.
- b) Some theoretical experience only from coursework, Linear Models WS)
- c) Some practical experience I have run a model for my research.
- d) Experienced I have run a number of models on different data.
- e) Very experienced I use models routinely.

# What is a model?



"All models are wrong, but some are useful" – George Box

From Research Essentials – Analysing your Data General Research Workflow

- 1. Hypothesis Generation
- 2. Experimental and Analytical Design (sampling, power, ethics approval)
- 3. Collect/Store Data
- 4. Data cleaning
- 5. Exploratory Data Analysis (EDA)
- 6. Data Analysis aka inferential analysis
- 7. Predictive modelling
- 8. Publication



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## **Workflow: Steps in Model Building**

- **1. Experimental and Analytical Design**
- 2. Data Cleaning
- 3. Exploratory Data Analysis (EDA)
- 4. Data/Inferential Analysis for Interpretable Models

### Fit a single model LM1/2/3, Survival analysis

- 1. Check model assumptions
- 2. Check goodness-of-fit
- 3. Interpreting Model Parameters and reach a conclusion

### Iterative Model building

Pick predictors to fit and a suitable modelling method based on EDA
Iteratively fit and assess models using predetermined strategy

### 5. Publication/Report

# So, let's dive into the workflow:

Assuming you have established your research question/ hypothesis, the next step is to do...

## 1. Experimental and Analytical Design – Model building

Decide on the aim of your model

Create an analysis plan and specify your Model Building Strategy

**Tip:** A sound study design and analysis plan increase your chances of grant success and high impact publications! Consider the SCU @SIH *Experimental Design* and *Power* + *Sample Size w*orkshops.



## Aim of Model Building – what is the 'best fit'?

## What is the purpose of your model? To make an inference to...

- 1. Gain knowledge interpret the relationships between predictors + outcome
  - get the most precise estimates be careful of interaction and confounding
  - Consider the level of subject matter knowledge/theory:
    - Fitting an a priori defined theoretical model needs strong theory/ controlled experiment – aim is hypothesis testing/ causal inference
    - Fitting different models to find the best one (some theory)
    - Fitting different models to create hypotheses (weak theory)
- 2. Predict future observations
  - Best model fit/ most accurate predictions
  - Interpretable test hypotheses about predictors that may be modifiable
  - If interested in prediction only, may use some Machine Learning approaches without making assumptions/ interpretations

# **Other Model aim considerations**

## Subject matter knowledge

- Consider ease of measurement and reliability of variables

## Parsimony/ Occam's Razor

- But include design variables/

known confounders/effect modifiers



title: "Core Principles" - originally published 10/12/2009

Create an analysis plan and specify your Model Building Strategy

- a) Identify the outcome variable and a full set of predictor variables to be considered
- b) Pick a suitable modelling method
- c) Specify the criterion (criteria) to be used in selecting the variables to be included
- d) Specify the strategy for applying the criterion (criteria)
- Determine potential/known confounders based on theory
- Determine interactions of interest



# Analysis plan: Identify the outcome variable and a full set of predictor variables to be considered – the full or maximal model

# Consider the outcome variable and all possible predictors of interest (justify using literature and unpublished data)

- Consider that administrative data is not designed for/ collected for research purposes
- Include 'design variables' depends on study design and type, controlled versus observational, e.g.
   block in RCT, exposure of interest, 'cluster' variables like students in classes within schools or hospitals or farms and potential confounders see our 'Experimental design' workshop for more information
- Consider potential confounders e.g. age, sex, BMI, SES, comorbidity, previous experience
- Consider what interaction terms to include

## This is as much a scientific/clinical task as it is a statistical task.



**Tip:** Documenting the justification for predictor inclusion + relevant references at the design stage will improve your design and make writing the discussion of your paper much easier!

## Analysis plan: Identify a full set of predictor variables – other strategies

### **Causal inference**/ strong theory:

If you have strong theory in your area of study, consider the causal structure of your data and data generating process (include sampling and unmeasured variables).

Consider how you can show causation, e.g. using Bradford-Hill criteria; by drawing a diagram for predictor variable inclusion/ causal inference (Directed acyclic graph – DAG, see appendix and tutorial+ references <u>here</u>)



## Analysis plan: Identify a full set of predictor variables – other strategies

If you have a large number of predictors you may want to:

## - Use univariable screening - weak theory/ exploratory:

Start with univariable screening with a liberal p value, e.g. p<0.2 or p<0.25 and re-test excluded predictors with the final model to ensure you did not miss important confounding; or

- Work in blocks, e.g. all demographic variables first and separately all clinical variables; then combine important predictors in the final model
- For multi-level models consider variables at **different levels separately** e.g. hospital-level factors versus individual-patient-level factors and enter variables meeting certain criteria from each level cumulative into a final model.

### Analysis plan: Identify a full set of predictor variables - Interactions

### Decide what interactions between predictors are to be considered

- Consider multiple testing adjustment if using large number of interactions see Linear Models 3 WS
- Evaluate interactions graphically where possible.
- Rule of thumb: Having more than two interaction terms usually over-complicates the model/ interpretation and may not represent reality – so avoid 3-way interactions unless indicated by the subject matter

### Five general strategies for creating and evaluating interactions\*:

- 1. Create and evaluate all 2-way interaction terms (ok for number of predictors <=8)
- 2. Create 2-way interactions among all predictors that are significant in the final main effects model (after model building)
- 3. Create 2-way interactions among all predictors found to have an unconditional (univariate) association with the outcome.
- 4. Create 2-way interactions only among pairs of variables which you suspect might interact (based on literature, expert knowledge etc), e.g. those involving the primary predictor of interest and important confounders.
- 5. Only create 2-way interaction terms that involve the predictor of interest.

### \* May be adjusted for 'biologically plausible' interactions only.



## Analysis plan: Identify a full set of predictor variables - piffalls

Over-fitting the data - too many predictors, not enough data/sample size.

## Rule of thumb: one should have at least 10 data points for each estimate, better 20

- For logistic regression/ survival analysis one should have at least this number of events
- An intercept needs an estimate/ regression coefficient; Interaction terms need estimates including main effects; categorical variables with more than two groups need multiple.

# If the goal is to create knowledge then we need our estimates to be as precise as possible – too little data will lead to large confidence intervals.

A large maximum model should include all potentially important predictors but it increases the chance of multicollinearity, unstable estimates and finding spurious associations that are not important in the real world or are difficult to interpret. Consider a focused study design collecting high quality data on far fewer predictors versus administrative 'big' data not collected for research purposes.

**Take home:** Consider sample size as part of your study design/analysis plan to ensure your model is sufficiently powered! See our *Power and Sample Size* workshop for more information.

## Analysis plan - Pick a suitable modelling method

### Outcome variable:

Its data type indicates which types of models may be used

See our specific workshops for more information on different models, e.g.:

- Linear Models 1 (numeric outcome)
- Linear Models 2 (binary outcome or count data)
- Survival analysis (time-to-event data).

How to decide which variables to keep in the model?

Selection criteria are formal 'Goodness of Fit' criteria and other statistical considerations

**Other statistical considerations -** retain variables that are:

- a primary predictor of interest
- a priori confounders for the primary predictor of interest
- Shown confounders for the primary predictor of interest (should not be an intervening variable see appendix)
- A component of an interaction term included in the model (for interpretation)

### Formal Goodness of Fit criteria – nested models

Nested models are based on the same set of observations (n) and the predictors in one model are a subset of predictors in the other model

Tests based on nested models to evaluate significance of a predictor:

- Partial F test (linear model)
- Wald test or likelihood ratio test (LRT) (other types of regression such as logistic, Poisson) – Wald test often most convenient, but LRT has best statistical properties and should be used if p value or standard error are questionable

### Formal Goodness of Fit criteria- non-nested models

Akaike's Information Criteria (AIC): alpha = 2

Bayesian Information Criteria (BIC) alpha = log n (with some variation)

### AIC/BIC:

- Assess overall model so can be used to compare different models
- The smaller the IC, the better the model
- Can be used to compare nested and non-nested models
- Can be used to compare different regression models, e.g. linear vs Poisson
- Can't be used to compare models based on different sets of observations
- Can't be used to compare models with different likelihood computation, e.g. Cox semiparametric survival model versus Weibull parametric model
- BIC depends on n and it can be unclear what n to use for clustered data
- BIC favours most parsimonious model

| Absolute<br>difference in AIC | Absolute<br>difference in BIC | Evidence for superiority of the better model |  |
|-------------------------------|-------------------------------|--|--|
| 0- <4                         | 0 - <2                        | Weak   |  |
| 4- <7                         | 2- <6                         | Positive                                     |  |
| 7 - <10                       | 6 - <10                       | Strong                                       |  |
| =>10                          | => 10                         | Very strong                                  |  |

Two additional approaches for linear regression models:

R squared - amount of variance explained by a univariable model Adjusted R squared = amount of variance explained by a multi-variable model, penalised for model complexity/number of predictors (larger is better)

- Avoids including predictors that explain a small amount of variance only
- Maximising R squared, minimises mean square error (MSE)

Mallow's Cp Statistic (special case of AIC) : Cp = Sum((Y-Y\_hat)^2)/sigma^2) - n + 2k

# Analysis plan: Specifying the selection strategy

How to get from a full/maximal model (all predictors selected for model building) to the final model?

 $\rightarrow$ Choose a selection strategy to build a model

- Manual options
- Automated processes
- Other considerations

## Analysis plan: Specifying the selection processes – the options

### All possible:

Examine all possible combinations of predictors.

### Best subset:

Software identifies 'best' model of all possible based on criteria (e.g. a model with 2 predictors, largest adjusted R squared; a model with 3 predictors, largest adjusted R squared)

#### **Forward** selection

First a model with only the intercept is fitted and then each variables is added selectively based on a specified criterion, e.g. having the largest Wald test statistic provided it corresponds to p<0.05 (or other chosen significance level). The predictor with the largest Wald test statistic is added first and then the process is repeated and continues until no term meets the entry criterion.

#### **Backward** elimination

As for forward selection but the process is reversed and model building starts with the full/maximal model. Predictors are removed sequentially until none of the predictors remaining in the model has a Wald test statistic meeting the specified criterion.

## Analysis plan: Specifying the selection process – the options

### Stepwise regression

A combination of forward selection and backward elimination.

Forward stepwise starts with forward selection but after the addition of each variable, the criterion for backward elimination is applied to each variable in the model to see if it should remain.

Backward stepwise starts with a full/maximal model and sequentially removes predictors but after the removal of each variable, all removed variables are checked to see if any of them would meet the forward selection criteria for inclusion.

Stepwise methods are critisised by some to be data dredging/ fishing approaches.

## So, what strategy to choose?



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## Analysis plan: Variable selection process - comparison

|       | Selection strategy | Comment  |  |
|-------|--------------------|--|--|
|       | All possible       | Good for early exploratory work with few predictors to find<br>multiple good model candidates. Can compare nested and non-<br>nested models.   |  |
|       | Best subset        | Researcher identifies when increasing the number of predictors<br>brings little predictive improvement. Can compare nested and non-<br>nested models.  |  |
|       | Forward            | Supports start simple, get complex – understanding at each step.<br>Can assess a priori confounders. May miss an important<br>confounder   |  |
|       | Backwards          | Statistical significance of terms is assessed after adjustment for<br>potential confounders; useful for smaller number of variables e.g.<br>several demographic that are likely confounding. |  |
|       | Forward stepwise   | Useful for large number of predictors/interaction terms.   |  |
| The U | Backwards stepwise | Generally favoured over forward stepwise.  |  |

# Analysis plan: Specifying the selection strategy

### Automated approaches:

Be cautious! While convenient, they should be considered exploratory methods rather than definite approaches.

- some journals will no longer accept automated selection
- They yield R squared values that are too high
- Based on Hypotheses tests p values too small and not adjusted for multiple testing → see LM3 Workshop
- Ignore multi-collinearity important to do your EDA/ correlation analysis!! Use VIF after model building to check.

### - DO NOT incorporate other statistical criteria:

Select 'design' variables/predictor a priori, e.g.

- Predictor variable of interest for the research question
- Randomisation blocking factor in an experiment
- A priori confounder of the predictor variable of interest

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# Model building strategy styles (adapted from Keith McCormick)

|                                   | Hierarchical                                | Simultaneous  | Stepwise   |
|-----------------------------------|---|---|--|
| Style                             | most academic                               |   | least academic                                       |
| Theory                            | Strong theory                               | Limited theory  | no theory  |
| Analyst role in model<br>building | choose variables, and<br>the order of entry | choose a list of<br>variables believed to<br>be important | Variables are chosen<br>through automated<br>process |
| Possible use                      | Designed experiments                        | Exploratory   | Data mining type<br>approach                         |

Source: LinkedIn Learning video: Three regression strategies, Keith McCormick.



## Collett's general strategy for model selection:

- 1. Fit univariate models for each predictor variable of interest. Compare the -2loglikelihood values to the null model (using chi square statistic, or AIC, BIC)
- 2. Significant variables from step 1 are fitted in a single model and compared to 'leave one out' models
- 3. Variables omitted at step 1 are then added to the best model from step 2 and compared
- 4. A final check to ensure no term in the model can be omitted without increasing -2LL significantly and no new term added without reducing -2LL significantly.

# Pitfalls with automated selection processes:

Avoids researcher thinking about their data and taking responsibility for their analysis!

## "Start Simple – Get Complex"

## "Every model you run tells you a story. Stop and listen to it."

- Avoid Overfitting (have at least 10 (better 20!) observations per parameter in the model keep in mind dummy coded categorical variables with > 2 categories e.g. a predictor with 5 categories requires 4 parameters to be estimated)
- For interpretability of parameters keep the main effects of both variables that make up a significant
   2-way interaction term in the model (irrespective of their p values)
- Analysis will only be based on observations for which all variables are not missing (with many missing observations the final data set analysed may be a small subset) – do EDA!

## Workflow: Steps in Model Building so far

### **1. Experimental and Analytical Design**

- Decide on the aim of your model
- o Create an analysis plan and specify your Model Building Strategy

### 2. Data Cleaning

### Step 2: Data Cleaning

For each variable including the outcome: identify the data type (numeric/categorical) and use appropriate summary statistics and plotting to check the distribution:

- Numeric variable histogram/boxplot; mean, median, standard deviation, percentiles, etc.
- Categorical variable bar charts; frequency tables with count and percent
- For model building we want variables that:
  - are measured accurately, precisely + are reasonably complete (not too much missing data, e.g. no more than 10-15% missing observations)
  - have substantial variability (e.g. if 99% are male, than sex is not a good predictor)

Categorical variables: consider combining categories with small number of observations/ eliminate.



See our Research Essentials – Analysing your Data Workshop for further details
## Workflow: Steps in Model Building so far

#### 1. Experimental and Analytical Design

- Decide on the aim of your model
- o Create an analysis plan and specify your Model Building Strategy
- 2. Data Cleaning
- 3. Exploratory Data Analysis (EDA): Pick predictors to fit and a suitable model using EDA

Assess relationships between each predictor and the outcome

Assess the relationships among predictors and consider variable reduction

## Step 3: Pick predictors to fit using Exploratory Data Analysis (EDA)

# **3.1** Assess relationships between each predictor and the outcome to select, modify + understand predictors

Plot the relationship of each predictor with the outcome – see *Research Essentials* 







2 categorical variables - side-by-side bar charts The University of Sydney

1 categorical, 1 numeric variable - side-by-side boxplots 2 numeric variables – xy scatter plot

### **Step 3: Pick predictors to fit using Exploratory Data Analysis (EDA)**



**For numeric variables in linear regression – assess the assumption of linearity** – is the relationship between outcome and predictor a line, a curve or something else?

For practical reasons we assess the model assumption of linearity before model building – see *Linear Models* workshops.



Alternatively, avoid the assumption by categorising the numeric predictor, but this loses information and may introduce bias. However, sometimes we are interested in specific categories for interpretation, e.g. BMI – underweight/normal weight/ overweight/obese.



Step 3: Pick predictors to fit and a suitable model using Exploratory Data Analysis (EDA)

**3.1** Assess relationships between each predictor and the outcome

3.2 Assess the relationships among predictors and consider variable reduction

## WHY is EDA so important??

*"Knowledge without practice is useless; practice without knowledge is dangerous."* Confucius

# A case study...



## Consider results from a multivariable model for Math test score...

|             | Estimate | Std. Error | t value | P value    |
|-------------|----------|------------|---------|------------|
| (Intercept) | 2.105    | 1.104      | 1.9     | 0.0569     |
| IQ          | 0.997    | 0.006      | 151.9   | <0.001***  |
| verbal.IQ   | -9.995   | 0.067      | -148.3  | < 0.001*** |

Multiple R-squared: 96%

$$y = b_0 + b_1 x_1 + b_2 x_2$$

Math test score = 2.1 + 1\*IQ - 10\*verbal.IQ

### What is your interpretation? Is this a good model?

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## EDA for verbal IQ and Math test score:



- EDA: correlation  $r=0 \rightarrow$  there is no relationship!
- MV Model: on average with a 1 point increase in verbal IQ, Math test score decreases by 10 points!

# Start Simple – Get Complex: use Exploratory Data Analysis (EDA) to assess the relationships among predictors and consider variable reduction

Numeric predictors: use xy scatter plot and conduct pairwise correlation analysis 'High' correlation is domain-specific, generally r>|0.7|, |0.8|or |0.9| but r<0.7 can be problematic too Only use one of a pair of highly correlated variables for multivariable modelling – WHY?





## **Simulated data**

math.IQ <- rnorm(1000, 60, 10)
math.test.score <- math.IQ + rnorm(length(math.IQ),0,2)</pre>

verbal.IQ <- rnorm(1000, 80, 5)

IQ <- 10\*verbal.IQ + math.IQ

math.test.score is math.IQ with a bit of noise

- $\succ$  IQ is a sum of verbal IQ and math.IQ (IQ:verbal.IQ r = 0.98)
- A model with verbal.IQ and IQ can re-arrange itself to: Math.IQ = IQ - verbal.IQ

# **Example summary**

**Results:** 

- Verbal IQ is not negatively correlated with Math Test Score as shown by the simple marginal model and the simulated data
- Yet a model with Verbal IQ and IQ suggests Verbal IQ is negatively corelated with Math Test Score.
- WHY: because IQ=verbal IQ + math IQ meaning a model which has both IQ and verbal IQ (which are correlated) can rearrange itself as math IQ = IQ verbal IQ.
- This a reversal of verbal IQ verbal IQ is **SUPRESSING** IQ (the part of IQ that is uncorrelated with Math results).
- This is an example of the reversal paradox due to multi-collinearity this may be called Simpson's paradox, Lord's paradox, and suppression - depending on whether the outcome and explanatory variables are categorical, continuous or a combination of both
- This is why we always look for multi-collinearity during the Exploratory Data Analysis using a scatterplot matrix to learn about the relationships between variables.

#### → Start Simple – Get Complex!

### **Relationships between variables - Correlation**



#### Why is 'high' correlation an issue for model building?

When interpreting the model, we make an assumption that the predictors are 'independent'.

# What is correlation? This is NOT it!! X1, x2 and x3 are statistically independent. No conditional effects – effects the same as in univariate analysis. The University of Sydney correlation r=0 Page 47

#### **Relationships between variables - Correlation**



Moderate correlation: there is overlap, but conditional effects are still interpretable. correlation r=0.5

#### **Relationships between variables - Correlation**



#### High correlation: x1 and x2 are almost identical

## correlation r=0.9

# The effect of high correlation: Example: $y \sim x1 + x2$



# Effect of high correlation/multi-collinearity on modelling

| Extent of<br>Multicollinearity | Effect on the Regression Analysis  |
|--------------------------------|--|
| Little                         | Not a problem  |
| Moderate                       | Not usually a problem  |
| Strong                         | Statistical consequences: Often a problem if you want to estimate effects of individual X variables (ie, regression coefficients); may not be a problem if your goal is just to predict or forecast $\gamma$ |
| Extremely<br>strong            | Numerical consequences: Always a problem; computer calculations may even be wrong due to numerical instability   |

# Potential indicators of multi-collinearity:



- Coefficients have signs opposite to what you'd expect from theory (suppression see DAG in appendix for explanation)
- Very high standard errors for regression coefficients
- Overall model is significant, but none of the coefficients are
- Large changes in coefficients when adding predictors
- Coefficients on different samples are wildly different
- High Variance Inflation Factor (VIF) and low tolerance (VIF reciprocal) direct measure of how much the variance of the coefficient is being inflated due to multicollinearity – e.g. linear combinations of variables correlated with a variable
- High condition index in PCA ratio between first and last PC

## For further information see:

https://www.theanalysisfactor.com/eight-ways-to-detect-multicollinearity/

#### **Step 3: Pick predictors to fit using Exploratory Data Analysis (EDA)**

#### 3.2 Assess the relationships among predictors and consider variable reduction

#### High pairwise correlations – what to do?

- If few variables: select only one of the pair based on biological plausibility, fewer missing values, ease/reliability of measurement or lower univariate p value (may not fix problems arising from collinearity among linear combinations of predictors --> also check Variance Inflation Factors (VIF) after analysis)
- If many (related?) predictors: explore their relationship/consider reducing the number of variables by using multivariate techniques - see our Multivariate
   Statistical Analysis 1 workshop
- Summarise the variables by creating an index/scale

## **Multivariate analysis -** Principal component Analysis + Factor Analysis

Principal component Analysis (PCA) and Factor Analysis (FA) are data reduction techniques to consolidate the information contained in a set of numeric predictor variables into a new set of fewer, uncorrelated

variables. If used subsequently in a model one cannot statistically test individual predictors.



Creates one or more index variables (components) from a larger set of W<sub>1</sub>

variables by using linear combinations (basically a weighted average) of a set of variables.

Component coefficients from a subsequent model can be backtransformed into coefficients for the original predictors – these are more stable as multi-collinearity is avoided.

#### FA:

PCA:

-Models the measurement of a latent variable which cannot be directly measured with a single variable, e.g. intelligence, statistical anxiety etc. -For subsequent modelling, determining which original predictor is important is subjective based on high correlations/factor loadings.

See SIH Multivariate Statistical analysis 1 workshop.

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## Multivariate analysis - Correspondence analysis



- A form of exploratory data analysis (EDA) designed to analyse the relationships among a set of categorical predictor and outcome variables
- Produces a visual summary which is a scatter plot with factorial axes that reflect the most variability in the original predictor variables
- Allows identification of clusters of predictors that are closely associated, with clusters further from the intersection of the axes having stronger associations

#### Summary:

PCA/FA and correspondence analysis are complementary techniques to modelling and provide insight into relationships between groups of predictors and there association with the outcome



# Create an index or scale



# Combine a number of related predictor variables into a single index

- Subjectively, ideally based on prior research can have different weights for different contributing factors, e.g. an infection control index may be created by counting the number of hygiene practices performed and expressing this as a percentage of all practices. This could also be categorised into low/medium/high.
- Objectively, e.g. fan capacity, size and number of air inlets and building size may be used to calculate the number of air changes per hour which could also be expressed as proportion of recommended ventilation level
- When predictors are assumed to be reflective of an underlying, unmeasured characteristic (a latent variable) can combine into index or scale by summing or averaging predictors and use Cronbach's alpha statistic to evaluate internal consistency of the scale. Use correlation analysis to assess correlation between each item (variable) and the scale and pairs of items to identify any items that do not fit into the scale well.
  - See SIH workshop on **Surveys' 2** for further information

## Create an index or scale - Comorbidity



#### **Definition:**

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Comorbidity is defined as the co-occurrence of one or more disorders in the same patient either at the same time or in some causal sequence and a common confounder

- Indices are calculated (weighted sum) from international ICD-10 diagnoses codes (+/- other data) from administrative data (e.g. admitted patients data)
  - Indices are based on Elixhauser, the Charlson/Deyo, and the Charlson/Romano methods and well-established for risk adjustment and mortality prediction
  - Calculation in R software: <u>comorbidity package –</u> <u>Rdocumentation</u>

#### Charlson comorbidity index

| Condition                     | Points in CCI |
|-------------------------------|---------------|
| Myocardial Infarction         | 1             |
| CHF                           | 1             |
| Peripheral Vascular Disease   | 1             |
| Cerebrovascular Disease       | 1             |
| COPD                          | 1             |
| Dementia                      | 1             |
| Paralysis                     | 1             |
| Diabetes                      | 1             |
| Diabetes With Sequelae        | 2             |
| Chronic Renal Failure         | 2             |
| Various Cirrhodites           | 1             |
| Moderate-Severe Liver Disease | 3             |
| Ulcers                        | 1             |
| Rheumatitis                   | 1             |
| AIDS                          | 6             |
| Any Malignancy                | 2             |
| Metastatic Solid Tumor        | 6             |

## Step 3: Pick a suitable model and predictors to fit using EDA

3.2 Plot the data in relation to the research question, e.g. Plot multiple variables in one plot; plot variables over time

## Parallel lines: consistent effect

## Non parallel lines: inconsistent effect $\rightarrow$ add interaction

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Supplement has no impact on feed's relationship with weight



Supplement has an impact on feed's relationship with weight





## Step 3: Pick a suitable model and predictors to fit using EDA

Plot data for individuals:

The difference between the 10 people (id) is much bigger than the effect of treatment.

→ To account for the variation between people we use a **random effect** for person in a mixed model – this makes our model more accurate and the estimate of treatment effect more precise.





## Step 3: Pick predictors to fit using Exploratory Data Analysis (EDA) - Summary

#### EDA for selection/modification of predictor variables for model building:

#### 3.1 Assess relationships between each predictor and the outcome

- Plot relationships and consider excluding variables with low variability
- Assess assumption of linearity for numeric predictors- see *Linear Models* workshops

#### **3.2** Assess the relationships among predictors and consider variable reduction

- Check for multi-collinearity and only select unrelated variables into model building
- Consider using univariable screening to reduce the number of variables for model building
- Look for patterns/structure in your data, e.g. interaction/ repeated measures

### R code/ resources for data cleaning and EDA



#### R code: EDA

- Introductory R and visualisation for EDA: R-essential-training-wrangling-and-visualizing-data

- Data management and summaries with R tidyverse: Learning the R Tidyverse

(These two LinkedIn Learning course are free with your Sydney uni login details)

#### R correlation matrix example:

# Create/simulate data
math.IQ <- rnorm(1000, 60, 10)
verbal.IQ <- rnorm(1000, 80, 5)
IQ <- 10\*verbal.IQ + math.IQ
math.test.score <- math.IQ + rnorm(length(math.IQ),0,2)
my\_data <- data.frame(math.IQ, verbal.IQ, IQ, math.test.score)</pre>

# install Ggally package and run ggpairs on all numeric variables (in this example all four variables are numeric)
install.packages("GGally")
library(GGally)
ggpairs(my\_data)

## Workflow: Steps in Model Building so far

- **1. Experimental and Analytical Design**
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#### Fit a single model LM1/2/3, Survival analysis

- 1. Check model assumptions
- 2. Check goodness-of-fit
- 3. Interpreting Model Parameters and reach a conclusion

#### Iterative Model building

 Pick predictors to fit and a suitable modelling method based on EDA
 Iteratively fit and assess models using predetermined strategy

# Step 4: Data/Inferential Analysis – Model Building

- a) Use iterative model building and determine final multivariable base model + check assumptions and goodness-of-fit
- b) Check interactions of interest with final base model if this strategy was prespecified
- c) If screening used: reassess eliminated predictors by adding one-by-one to final model
- d) Assess models: enumerate level of confounding calculate % change in estimate
- e) Interpret model building strategy: determine final, final model consider sensitivity analysis (e.g. model with and without potential confounder when p>0.05)
- f) Prediction rank models in order of predictive ability

## **Step 4: Inferential Model building**

#### - An iterative process

 Fit and evaluate models based on predefined criteria and strategy

## **Consider changing strategy** if:

- issues with sampling/ optimal sample size not reached
- EDA indicates modelling method not suitable

|        |                                   |        |      |         |    |      |        | 95.0% CI1 | or Exp(B) |
|--------|-----------------------------------|--------|------|---------|----|------|--------|-----------|-----------|
|        |                                   | В      | SE   | Wald    | df | Sig. | Exp(B) | Lower     | Upper     |
| Step 1 | Age at hospital<br>admission      | .066   | .006 | 118.799 | 1  | .000 | 1.068  | 1.056     | 1.081     |
| Step 2 | Age at hospital<br>admission      | .059   | .006 | 92.407  | 1  | .000 | 1.060  | 1.048     | 1.073     |
|        | Congestive heart<br>complications | 861    | .142 | 36.570  | 1  | .000 | .423   | .320      | .559      |
| Step 3 | Age at hospital<br>admission      | .059   | .006 | 92.280  | 1  | .000 | 1.061  | 1.048     | 1.074     |
|        | Cardiogenic shock                 | 883    | .261 | 11.414  | 1  | .001 | .413   | .248      | .690      |
|        | Congestive heart<br>complications | 820    | .143 | 32.745  | 1  | .000 | .440   | .332      | .583      |
| Step 4 | Age at hospital<br>admission      | .060   | .006 | 90.699  | 1  | .000 | 1.061  | 1.048     | 1.074     |
|        | hr                                | .009   | .003 | 10.649  | 1  | .001 | 1.009  | 1.004     | 1.015     |
|        | Cardiogenic shock                 | 959    | .261 | 13.464  | 1  | .000 | .383   | .230      | .640      |
|        | Congestive heart<br>complications | 707    | .147 | 23.109  | 1  | .000 | .493   | .370      | .658      |
| Step 5 | Age at hospital<br>admission      | .054   | .006 | 71.465  | 1  | .000 | 1.055  | 1.042     | 1.069     |
|        | hr                                | .012   | .003 | 16.723  | 1  | .000 | 1.012  | 1.006     | 1.018     |
|        | initial diastolic BP              | 012    | .003 | 11.022  | 1  | .001 | .989   | .982      | .995      |
|        | Cardiogenic shock                 | -1.052 | .264 | 15.875  | 1  | .000 | .349   | .208      | .586      |
|        | Congestive heart<br>complications | 690    | .147 | 22.087  | 1  | .000 | .501   | .376      | .669      |
| Step 6 | Age at hospital<br>admission      | .048   | .007 | 52.485  | 1  | .000 | 1.049  | 1.036     | 1.063     |
|        | hr                                | .012   | .003 | 16.746  | 1  | .000 | 1.012  | 1.006     | 1.018     |
|        | initial diastolic BP              | 011    | .004 | 9.952   | 1  | .002 | .989   | .982      | .996      |
|        | BMI                               | 046    | .016 | 8.059   | 1  | .005 | .955   | .926      | .986      |
|        | Cardiogenic shock                 | -1.099 | .265 | 17.199  | 1  | .000 | .333   | .198      | .560      |
|        | Congestive heart<br>complications | 692    | .146 | 22.319  | 1  | .000 | .501   | .376      | .667      |
| Step 7 | Gender                            | .294   | .144 | 4.190   | 1  | .041 | 1.341  | 1.013     | 1.777     |
|        | Age at hospital<br>admission      | .050   | .007 | 56.392  | 1  | .000 | 1.051  | 1.038     | 1.065     |
|        | hr                                | .012   | .003 | 18.357  | 1  | .000 | 1.013  | 1.007     | 1.018     |
|        | initial diastolic BP              | 012    | .003 | 11.281  | 1  | .001 | .988   | .982      | .995      |
|        | BMI                               | 048    | .016 | 8.530   | 1  | .003 | .953   | .923      | .984      |

#### Variables in the Equation

## Step 4: Inferential analysis - Check the model assumptions

Use "diagnostics" to assess the validity of the model – see Linear Models and Survival Analysis workshops e.g.

- Evaluate normality of residuals in LM
- Check HR/OR proportionality assumptions
- Check for influential values

## For multivariable models:

- Check the assumption of independent predictors using
- Variance Inflation Factors (VIF) for multi-collinearity among more than 2 predictors after analysis:
- VIF >4 moderate multi-collinearity
- VIF >10 strong multi-collinearity



# Step 4: Inferential Analysis - Check model fit

Evaluate the *reliability* of the model – how well will the model predict observations in future samples?

Different approaches, e.g.:

- Split-sample analysis
- Cross-validation
- Leave-one-out analysis
- Bootstrap



- Goodness-of-fit test, e.g. Hosmer-Lemeshow test

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#### 5. Publication/Report

# Step 5: Publication/reporting – interpret results

- Present point estimates the coefficients (including the intercept)
- Present the measure of uncertainty their standard errors and/or their confidence interval.

Depending on target audience, non-numerical presentation of study results may be preferable.



# Step 5: Interpret and report the results



#### Assessing the impact of continuous variables:

- Continuous variables are measured on different scales, so a 'one unit change' could be small or large.
- It is difficult to compare the impact of different continuous variables
- $\rightarrow$  use standardised coefficients (multiply by ratio of SD of predictor to SD of outcome)
- $\rightarrow$  compute and present a range of predicted effects as a continuous predictor changes over its IQR

| Variable   | Estimate | Basis       | Estimated<br>effect<br>change | Effect |
|------------|----------|-------------|-------------------------------|--------|
| Held-back  | 0.666    | dichotomous | O - 1                         | 0.666  |
| Herd size  | 0.669    | IQR         | 0.55-1.60                     | 0.702  |
| experience | 0.023    | IQR         | 8.5 – 26.0                    | 0.401  |

Modelling log-prevalence of respiratory disease in pigs

# Step 5: Interpret and report the results

#### Control of confounding at the analysis stage:

Use change in measure of association as an indication of confounding

Calculate % change between estimates for statistically significant predictor of interest with confounder in the model versus without confounder in the model

Include confounder as covariate in regression analysis; assess confounding effect by examining the % change in regression parameter estimate in a model with and without a (potential) confounder (see next slide for an example calculation).

Confounder are often included a *priori*, irrespective of p-value or the effect of its inclusion/exclusion on change in other parameters.

Assessment of confounding should be specified in your analysis plan and a "substantial difference" defined a priori, e.g. >20-30% change in log odds may be considered substantial confounding.

Remember: Don't forget to describe your treatment of confounders in the "Methods" section of your paper and report the results of your assessment in the "Results" section.

#### Step 5: Interpret and report the results – example results tables

Table 1: Univariable linear regression model results showing the association between offspring height with father's height, mother's height, gender and financial situation in a study of 288 university students conducted in Sydney.

| Variable                                 |                    | <u></u> | S.E.( $\widehat{b}$ ) | 95% CI         | P<br>value | Percentage<br>variance<br>accounted<br>for<br>(Adjusted<br>R <sup>2</sup> ) |
|--|--------------------|---------|-----------------------|----------------|------------|---|
| Constant                                 |                    | 90.0    | 12.3                  | (65.9, 114.1)  | <.001      | 13.7  |
| Father height                            |                    | 0.47    | 0.07                  | (0.33, 0.60)   |            |   |
| Constant                                 |                    | 71.4    | 14.3                  | (43.2, 99.6)   | <.001      | 15.1  |
| Mother height                            |                    | 0.62    | 0.09                  | (0.45, 0.79)   |            |   |
| Gender (reference=F                      | emale)             | 167.0   | 0.56                  | (165.9, 168.1) | <.001      | 46.8  |
|  | Male               | 13.98   | 0.88                  | (12.2, 15.7)   |            |   |
| Finance (reference=Finding it difficult) |                    | 171.5   | 1.17                  | (169.2, 173.8) | 0.147      | 0.8   |
|  | Just getting along | 0.33    | 1.69                  | (-3.00, 3.66)  |            |   |
|  | Comfortable        | 0.61    | 1.59                  | (-2.52, 3.74)  |            |   |
|  | Prosperous         | 3.63    | 1.73                  | (0.23, 7.03)   |            |   |

Going from a univariable model to a multivariable model with gender and father height, the effect of mother height decreases by 33%. = ((0.62-0.41)/0.62)\*100

Table 2: Final multivariable linear regression model for offspring height in a study of 288 university students in Sydney

| Variable  |                    | Estimate | S.E.  | 95% CI |       | P value |
|-----------|--------------------|----------|-------|--------|-------|---------|
| Intercept |                    | 24.70    | 10.20 | 4.71   | 44.69 | 0.016   |
| Mother_ht |                    | 0.41     | 0.05  | 0.31   | 0.52  | <.001   |
| Father_ht |                    | 0.42     | 0.04  | 0.34   | 0.51  | <.001   |
| Gender    | Male versus Female | 14.19    | 0.69  | 12.84  | 15.53 | <.001   |

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# Step 5: Interpret and report the results

# Predictors eliminated from a model – different options, particularly for exploratory observational studies:

- Eliminated predictors may be forced back into the final model one-by-one to check its effect if this method is used it should be specified in the analysis plan + paper methods section
- You may also want to discuss the potential effects of predictors not included in the model (alpha = 0.05 is an arbitrary cut-off and a predictor with p = 0.06 still shows evidence of a (weak) association different journals and statistical reviewers have different viewpoints on this some journals/ reviewers don't want them included (perceived as 'fishing'/ data dredging)
- For backward elimination the coefficients of the predictor at the last step before it was eliminated can be reported
- Observational studies: often one Table presents univariate results and one Table shows the final multivariable model (if there are a lot and/or journal does not want non-significant univariate results in the manuscript the univariate Table(s) can be presented in an appendix/ online supplementary file
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# A reminder about Acknowledging SIH 🛛 🗸

All University of Sydney resources are available to Sydney researchers **free of charge**. The use of the SIH services including the Artemis HPC and associated support and training warrants acknowledgement in any publications, conference proceedings or posters describing work facilitated by these services.

The continued acknowledgment of the use of SIH facilities ensures the sustainability of our services.

#### Suggested wording:

General acknowledgement:

"The authors acknowledge the statistical consulting service provided by the Sydney Informatics Hub, a Core Research Facility of the University of Sydney."

Acknowledging specific staff:

"The authors acknowledge the statistical consulting service provided by (name of staff) of the Sydney Informatics Hub, a Core Research Facility of the University of Sydney."

"The authors acknowledge the Statistical workshops and workflows provided by the Sydney Informatics Hub, a Core Research Facility of the University of Sydney."

## **Upcoming SIH statistical trainings**

Check out the SIH training calendar or sign up to the mailing list for details on all upcoming trainings:

https://www.sydney.edu.au/research/facilities/sydney-informatics-hub/workshops-andtraining/training-calendar.html

Consider our monthly informal "Hacky Hour" session for all your data management, visualization and coding queries:

Sydney Hacky Hour - The University of Sydney

### Further Assistance at Sydney University

#### SIH

#### - Workshops

This is just one workshop from a modular training programme made up of 1.5 hour workshops, each focusing on a single statistical method offered by Statistical Consulting within the Sydney Informatics Hub. Statistical Workflows giving practical step-by-step instructions applicable in any software are used and include experimental design, exploratory analysis, modelling, assumption testing, model interpretation and presentation of results. They are integrated into Training Pathways (insert link) to give a holistic understanding of data analysis from a statistical perspective. Researchers are also encouraged to design a custom programme tailored to their research needs.

Look for the statistics workshops (and other SIH workshops) on our training page <a href="https://www.sydney.edu.au/research/facilities/sydney-informatics-hub/workshops-and-training.html#stats">https://www.sydney.edu.au/research/facilities/sydney-informatics-hub/workshops-and-training.html#stats</a>.

- Statistical Resources from the Sydney Informatics Hub | stats-resources (sydney-informatics-hub.github.io)
- Training: Sign up to our mailing list to be notified of upcoming training: mailman.sydney.edu.au/mailman/listinfo/computing\_training
- Hacky Hour <u>www.sydney.edu.au/research/facilities/sydney-informatics-hub/workshops-and-training/hacky-hour.html</u> OR Google "Sydney Hacky Hour"
- 1 on 1 Consults can be requested on our website <u>www.sydney.edu.au/research/facilities/sydney-informatics-hub.html</u> OR Google "Sydney Informatics Hub"

#### OTHER

- Open Learning Environment (OLE) courses
- Linkedin Learning: <u>https://linkedin.com/learning/</u>
  - SPSS <u>https://www.linkedin.com/learning/machine-learning-ai-foundations-linear-regression/welcome?u=2196204</u>

## We recommend our Experimental Design and Sample Size Workshops

#### **Experimental Design Workshop**

- Far too many researchers think they know all they need to in this area. We commonly see designs that could be substantially improved for stronger causal inference and improved results which leads to publication in higher impact journals (amongst other benefits).
- Even if you have already collected your data it is well worth attending since it may improve your write up and analysis e.g. we had a client who didn't realise they had a very strong Before/After Control/Impact (BACI) design.

#### Sample and Power Workshop

- Shows the steps and decisions researchers need to make when designing an experiments to ensure sufficient sample e.g. Power, minimum required to fit the necessary model, etc.
- Also how much Power the study has i.e. does it have sufficient power to detect the effects you expect to see, or is your study a complete waste of time and resources.

### We value your feedback



We want to hear about you and whether this workshop has helped you in your research. What **worked** and what **didn't work**.

### We actively use the feedback to improve our workshops.

Completing this survey really does help us and we would appreciate your help! It only takes a few minutes to complete (promise!)

The link to the survey will be emailed.

## Appendix 1. DAG - a graphical aid to understand multivariable systems and relationships between variables 2. References used for development of this

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workshop

## What is a DAG?

- DAG (Directed Acyclic Graph) = causal diagram = modified path model
- Start with a plausible (biological) causal structure (data generating process DGP) and translate it into a graph with hypothesised and known relationships among variables
- Lines represent:
  - Arrow (directed edge) = (assumed) causal relationship
  - No arrow = no causal relationship

Example study aim: Identify factors of causal importance to pneumonia (lung disease)

Objective: Investigate the association of Strep infection and the occurrence of lung disease. Researchers also measured sero-conversion for COVID-19.

Streptococcus pneumoniae Infection - Strep



## **Relationship: Exposure-independent predictor variable**

### Causal model (DAG)



### Statistical model (Venn diagram)



The two predictor circles do not overlap – they are statistically independent.

Both overlap with the outcome indicating their significant statistical associations with Disease. A patient could have one infection, both infections or none. Page 81

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## Relationship: A simple antecedent predictor variable

### Causal model (DAG)

Covid  $\longrightarrow$  Strep  $\longrightarrow$  Disease

### Statistical model (Venn diagram)



There is weak overlap of Covid with the outcome but statistical association favour direct causes over indirect causes, so strength of association and significance of Covid may be low. The association of Strep and Disease would not change when the model is adjusted for Covid. Covid occurs before Strep infection making patients more susceptible – Covid may be very important for disease control!

Relationship: An explanatory antecedent variable – complete confounding

### Causal model (DAG)



### Statistical model (Venn diagram)



The Strep circle overlaps with the outcome, as they are statistically related until Covid is added to the model. Then the association becomes non-significant as all of the previous crude association is covered by the Covid-Disease association. Relationship: an explanatory antecedent variable – partial confounding

### Causal model (DAG)



### Statistical model (Venn diagram)



The Strep circle overlaps with the outcome. The association remains significant when Covid is added to the model but some of the previous association is now covered by the Covid-Disease association.

The Strep-Disease association is not as strong when Covid confounding is controlled but the model with both predictors explains more variation in Disease than just Strep.

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### More on confounding: a classic example



Age confounds the relationship of smoking and lung cancer – smoking may be more prevalent among older people and older people are more likely to get lung cancer irrespective of smoking.

Examples of common confounders:

Age, Sex, Socio-economic status, Comorbidity, previous experience, etc.

**Relationships: an intervening predictor variable** 

### Causal model (DAG)

#### Strep Covid Disease

### Statistical model (Venn diagram)



The Strep circle might or might not overlap with the outcome. However, any association of Strep with Disease disappears when Covid is added to the model. The effect of Strep on Disease is mediated by Covid. Adding Covid to the model would lead us to believe that Strep is not associated with Disease (and hence we may wrongly conclude that Strep is not a cause of Disease). Intervening variables should be identified and not be used/controlled when estimating the causal effect of an exposure  $\rightarrow$  consider Structural equation modelling, mediation analysis instead if interested in the mediator.

Relationship: a distorter predictor variable, can cause association reversal - one relationship represents prevention (-ve) rather than causal effect



Strep is a cause of Disease. Having Covid prevents getting Disease. Covid is positively correlated with Strep.

Causal model (DAG)



Strep and Covid are both causes of Disease. Having Covid prevents Strep infection.

In either case – need to control for the distorter variable Covid

#### Relationship: a suppressing predictor variable

### Causal model (DAG)



Strep and the suppressor Covid are both members of the same global variable 'Hospital contact' (a proxy variable for exposure to infectious agents)

### **Statistical model**



The variable 'hospital contact' has no or only weak unconditional association with the outcome. Once Covid is controlled in the analysis, the Strep circle overlaps with the outcome indicating an association of 'hospital contact' with Disease. By controlling the non-causal component of the global variable we reveal and strengthen the suppressed association of the remaining factor with the outcome. The global variable should be refined to exclude Covid. Suppression of the outcome can also occur, e.g. if the disease is not well defined (no association with lung disease but a strong association with a specific type of lung disease).

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Relationship: a moderator variable – statistical interaction

### Causal model (DAG)



absent (Covid -)

The Strep circle overlaps with Disease only when Covid is present. No disease occurs unless both predictors are present. Interaction has large implications for disease control. Moderators may or may not be confounders.

when Covid is present (Covid +)

## Summary of effects of extraneous variables

| Covid is a(n)<br>variable                          | Likely effect on<br>Strep coefficient<br>when adding<br>Covid | Comments   |
|--|---|--|
| Exposure independent                               | No change 📫   | Covid explains some of the Disease incidence, so the residual variance is smaller and significance of Strep increases.   |
| Simple antecedent                                  | No change 📄   | No effect on the analysis by Covid, but Covid might be important to know<br>about from a prevention perspective, e.g. if easier to address than Strep.   |
| Explanatory antecedent<br>(complete confounding)   | Becomes 0   | Control of Covid will remove any Strep association with Disease. R squared should increase as residual variance decreases.   |
| Explanatory antecedent<br>(incomplete confounding) | <b>S</b>  | Controlling Covid will impact on significance of Strep depending on the strength of Covid effect on Strep and disease. R squared should increase.  |
| Intervening  | <b>S</b>  | Because Covid is more closely related with Disease it probably has a<br>stronger association and explains more variability. Strep coefficient is<br>reduced in size and significance. If all effect passes through intervenor it<br>will remove Strep effect on Disease. |
| Distorter  | S 🖉   | Essentially same impact as explanatory antecedent except the Strep effect is increased or in opposite direction to the crude association.  |
| Suppresor  | <b>~</b>  | As the global variable containing Strep is refined, it will now have a stronger relationship with Disease and probably explain more variation.   |
| Moderator  | N/A   | With interaction the effect of one variable depends on the level of the other variable, hence separate estimates of effects are required.  |

RCT DAG – what is an 'instrumental' variable?

### **Example: A randomised Controlled Trial (RCT) experiment**



**Treatment:** Control group – not vaccinated Treatment group – vaccinated

Vaccination is an '**Instrumental variable**', it has direct causal effect on exposure, is unrelated to the outcome and shares no common cause with the outcome



## **References used when building this Workshop**

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## Model Building: R software resources



Linear model building example in R and other relevant resources for R: <u>https://r4ds.had.co.nz/model-building.html</u>