Directed acyclic graphs: what are they and what are they useful for?

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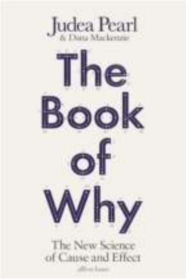
Outline

- Introduction
- Introduction to directed acyclic graphs (DAGs)
- *d*-separation rules
- Statistical independence
- Backdoor paths and confounding
- Examples
- Disadvantages of DAGs
- Discussion

Introduction I

- Alot of the theory developed in the late 1980s and 1990s (Pearl (1995))
- Hit mainstream only relatively recently (Munafò et al. (2018), Hèrnan (2017))
- Recent publicity, Pearl's Book of Why published this year



Introduction II

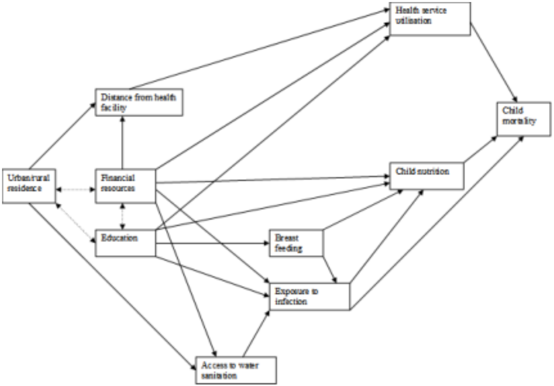
- Lots of interest in epidemiology, however . . . *DAG anxiety*

Introduction III

- The (old) rules of epidemiological modelling:
  - Adjust for common causes
  - Do not adjust for common effects
  - Do not adjust for variables on the causal pathway
- Easy to apply to simple situations with a few variables
- But how do we apply these when the model is (realistically) complex?

Introduction IV

- What should we adjust/not adjust for to estimate the effect of `Health service utilisation` on `Child mortality`?



Introduction to DAGs I

Causal

- A DAG is said to be causal for an effect if all common causes of the exposure and outcome are on the DAG

D: Directed

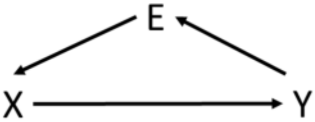
- DAGs depict structural relationships – causal effects without modelling assumptions
- Unlike SEM path diagrams they do not show residuals
- DAGs for different models are the same, e.g.
  - linear regression of Y on X, logistic regression of Y on X

$$X \longrightarrow Y$$

Introduction to DAGs II

A: Acyclic

- Following the direction of arrows from X we should not be able to get back to X
- This DAG is not allowed



- Intuition: the rules of conditional independence

Introduction to DAGs III

G: Graph

- Nodes represent variables
- Say we have this regression,

  $y_i = \beta_0 + \beta_1 x_i + \varepsilon_i, \quad \varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$
- Arrows represent effects (arrow from X to Y represents β_1)

$$\mathrm{X} \longrightarrow \mathrm{Y}$$

Path

- Any consecutive sequence of arrows (edges) regardless of the direction of the arrow

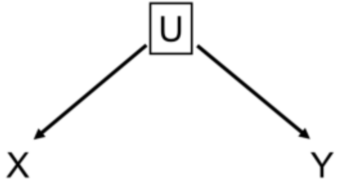
d-separation rules I

- *d*: directional
- Defined by Pearl (1995)
- Rule 1: if there are no variables being conditioned on, a path is blocked if and only if 2 arrows collide at some point on the path

- Because of the collider U we say X and Y are not *d*-connected
- *d*-connected: unblocked path between 2 variables (i.e. path with no collider)

d-separation rules II

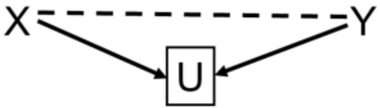
- Rule 2: Any path that contains a non-collider/common cause/confounder that has been conditioned on is blocked



- Conditioning/adjusted for/included in a model denoted by square box around variable

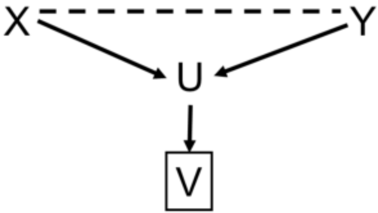
d-separation rules III

- Rule 3: A collider that has been conditioned on does not block a path



d-separation rules IV

- Rule 4: A collider that has a descendant that has been conditioned on does not block a path

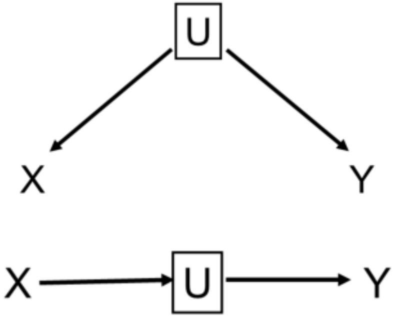


d-separation rules V

- If a pair of variables are *d*-separated they are statistically independent (conditional on any variables required to block backdoor paths between them)
- X and Y independent

d-separation rules VI

- X and Y independent given U; written as $X \perp\!\!\!\perp Y | U$



d-separation rules VII

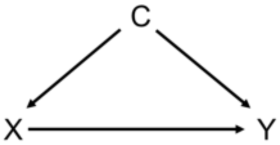
- Complex pathways now have a (hopefully) clearer interpretation

$$X \longrightarrow Z_1 \longleftarrow Z_2 \longleftarrow Z_3 \longleftarrow Y$$

- Are X and Y d-separated if we, condition on:
  - Z_1?
  - Z_2?

Backdoor paths and confounding I

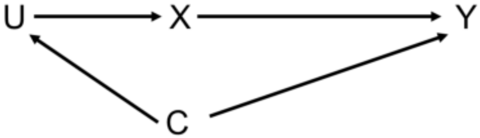
- A backdoor path starts by travelling the wrong way along an arrow



- X-C-Y is a backdoor path

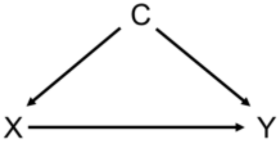
Backdoor paths and confounding II

- We can travel the wrong direction along an arrow more than once



- X-U-C-Y is a backdoor path

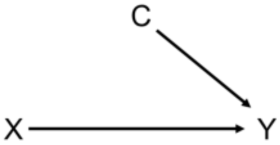
Backdoor paths and confounding III



- Here C fulfills conventional definition of a confounder, because it is:
  - associated with X (arrow C-X)
  - associated with Y conditional on X (arrow C-Y)
  - is not on the causal pathway between X and Y
- Structural definition of confounding: the existence of an open backdoor path between X and Y.

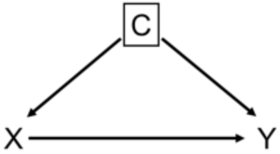
Backdoor paths and confounding IV

- In trials randomization removes C-X (X: randomized treatment) arrow



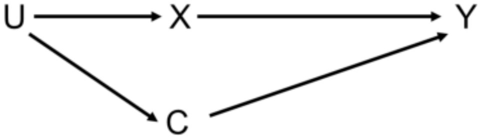
Backdoor paths and confounding V

- If we condition on C (e.g. include it as an additive covariate in model) then the path is blocked



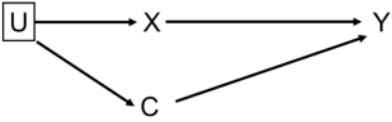
Backdoor paths and confounding VI

- In this DAG, to estimate the effect of X on Y what should we do?

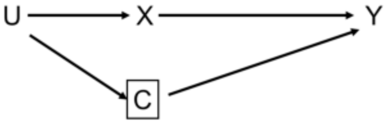


Backdoor paths and confounding VII

- We can adjust for U

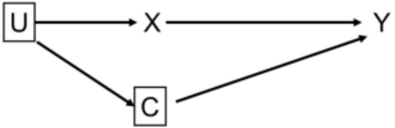


- We can adjust for C



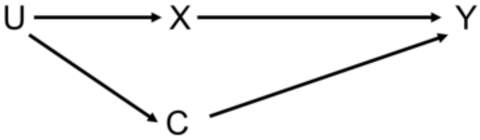
Backdoor paths and confounding VIII

- We can adjust for both U and C



Backdoor paths and confounding IX

- Defining a variable as a confounder is relative to which effect we are estimating
- To estimate the effect of U on Y what should we do?



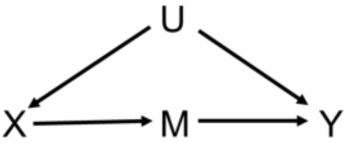
Backdoor paths and confounding X

- Say we propose the model:
  $y_i = \beta_0 + \beta_1 x_i + \beta_2 m_i + \varepsilon_i, \quad \varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$

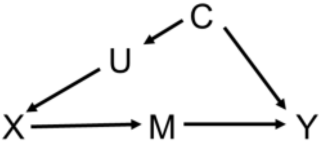
- If the estimate $\widehat{\beta}_1$ is found not to be null, we could have

Backdoor paths and confounding XI

- or

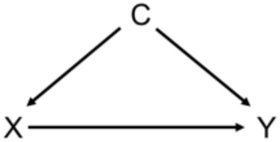


- or an even more complex confounding structure (or others)



Confounding example I

- Let's investigate what happens when we simulate some data
- Assuming linear models



- True model is: $y_i = \beta_0 + \beta_1 x_i + \beta_2 c_i + \varepsilon_i, \quad \varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$

Confounding example II

- Of course the unadjusted model is biased

```
set.seed(123456)
n <- 150
c <- rnorm(n)
x <- c + rnorm(n)
y <- c + x + rnorm(n)
lm(y ~ x) %>% summary() %>% coef()
```

```
##                Estimate Std. Error    t value     Pr(>|t|)
## (Intercept) -0.04430578 0.10116577 -0.4379522 6.620594e-01
## x            1.40874066 0.06933222 20.3187003 1.164942e-44
```

Confounding example III

- The true model is unbiased

```
lm(y ~ x + c) %>% summary() %>% coef()
```

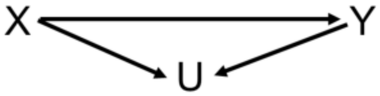
```
##                Estimate Std. Error     t value     Pr(>|t|)
## (Intercept) 0.001936471 0.08563298  0.02261361 9.819892e-01
## x           0.896588477 0.08808434 10.17875007 9.487072e-19
## c           1.008965959 0.12965362  7.78201172 1.164183e-12
```

```
lm(y ~ x + c) %>% confint.default()
```

```
##                  2.5 %   97.5 %
## (Intercept) -0.1659011 0.169774
## x            0.7239463 1.069231
## c            0.7548495 1.263082
```

Colliding example I

- If the DAG is



- Adjusting for U induces bias

```r
set.seed(123456)
n <- 150
x <- rnorm(n)
y <- x + rnorm(n)
u <- x + y + rnorm(n)
lm(y ~ x + u) %>% summary() %>% coef()
```

Colliding example II

```
##               Estimate Std. Error    t value     Pr(>|t|)
## (Intercept) 0.0428632 0.06130921  0.6991316 4.855745e-01
## x           0.1798452 0.10948445  1.6426553 1.025917e-01
## u           0.4611080 0.04530104 10.1787501 9.487072e-19
lm(y ~ x + u) %>% confint.default()

##                   2.5 %    97.5 %
## (Intercept) -0.07730064 0.1630270
## x           -0.03474037 0.3944308
## u            0.37231957 0.5498964
```

Colliding example III

- Fitting the correct model

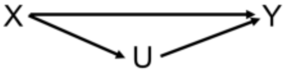
```
lm(y ~ x) %>% summary() %>% coef()

##               Estimate Std. Error    t value     Pr(>|t|)
## (Intercept) 0.07459585 0.07967631  0.9362362 3.506768e-01
## x           1.09975103 0.08041755 13.6755105 4.837012e-28
lm(y ~ x) %>% confint.default()

##                   2.5 %    97.5 %
## (Intercept) -0.08156685 0.2307585
## x            0.94213554 1.2573665
```

Mediation example I

- If the DAG is



- To estimate the direct effect of X on Y

```r
set.seed(123456)
n <- 150
x <- rnorm(n)
u <- x + rnorm(n)
y <- x + u + rnorm(n)
coef(summary(modelm <- lm(y ~ x + u)))
```

Mediation example II

```
##                Estimate Std. Error     t value     Pr(>|t|)
## (Intercept) 0.001936471 0.08563298  0.02261361 9.819892e-01
## x           1.008965959 0.12965362  7.78201172 1.164183e-12
## u           0.896588477 0.08808434 10.17875007 9.487072e-19
```

Mediation example III

- To estimate the total effect we fit

```r
lm(y ~ x) %>% summary() %>% coef()
```

```
##              Estimate Std. Error    t value     Pr(>|t|)
## (Intercept) 0.06881825  0.1111027  0.6194113 5.365978e-01
## x           1.99499006  0.1121363 17.7907659 1.379348e-38
```

Mediation example IV

- To estimate the indirect effect, first fit

```
coef(summary(mod1 <- lm(u ~ x)))
```

```
##               Estimate Std. Error    t value     Pr(>|t|)
## (Intercept) 0.07459585 0.07967631  0.9362362 3.506768e-01
## x           1.09975103 0.08041755 13.6755105 4.837012e-28
```

- Multiply the X-U and U-Y path coefficients

```
(indeff <- coef(mod1)[2] * coef(modelm)[3])
```

```
##         x
## 0.9860241
```

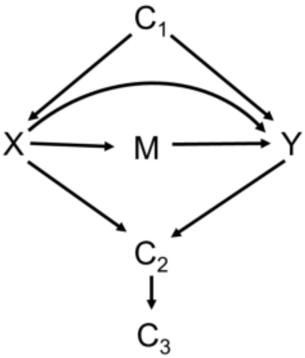
- Compare sum of direct and indirect effects to previous total effect

```
(toteff <- coef(modelm)[2] + indeff)
```

```
##       x
## 1.99499
```

More complex example I

- If the DAG is



More complex example II

```r
set.seed(123456)
n <- 150
c1 <- rnorm(n)
x <- c1 + rnorm(n)
m <- x + rnorm(n)
y <- c1 + x + m + rnorm(n)
c2 <- x + y + rnorm(n)
c3 <- c2 + rnorm(n)
```

More complex example III

- For the direct effect of X on Y of course the simple model is biased

```
coef(summary(modelx <- lm(y ~ x)))
```

```
##               Estimate Std. Error   t value     Pr(>|t|)
## (Intercept) 0.07280811 0.12618137  0.5770116 5.648083e-01
## x           2.37476121 0.08647624 27.4614312 5.805841e-60
```

More complex example IV

- Adjusting for C_1 and M recovers the direct effect as expected

```
lm(y ~ x + m + c1) %>% summary() %>% coef()
```

```
##              Estimate Std. Error   t value     Pr(>|t|)
## (Intercept) 0.1115822 0.07946580  1.404154 1.623967e-01
## x           1.0173919 0.10672719  9.532640 4.795425e-17
## m           1.0107777 0.07653848 13.206138 1.073170e-26
## c1          0.8796623 0.12031788  7.311151 1.609465e-11
```

More complex example V

- Adjusting for either C_2 or C_3 or both induces bias

```r
lm(y ~ x + m + c1 + c2) %>% summary() %>% coef()
```

```
##                Estimate Std. Error    t value     Pr(>|t|)
## (Intercept)  0.06511859 0.05925209  1.0990092 2.735855e-01
## x           -0.03128823 0.12467456 -0.2509592 8.022009e-01
## m            0.47786867 0.07501430  6.3703681 2.349755e-09
## c1           0.34870404 0.10186449  3.4232148 8.046834e-04
## c2           0.52432123 0.04807025 10.9073949 1.337696e-20
```

More complex example VI

- Adjusting for C_3

```
lm(y ~ x + m + c1 + c3) %>% summary() %>% coef()
```

```
##              Estimate Std. Error  t value     Pr(>|t|)
## (Intercept) 0.1080981 0.06351287 1.701987 9.090087e-02
## x           0.2389449 0.12053160 1.982425 4.932154e-02
## m           0.6772346 0.07122761 9.508036 5.841841e-17
## c1          0.5322631 0.10339923 5.147650 8.442526e-07
## c3          0.3557591 0.03891790 9.141270 5.073325e-16
```

More complex example VII

- Adjusting for both C_2 and C_3

```
coef(summary(fullmodel <- lm(y ~ x + m + c1 + c2 + c3)))
```

```
##                Estimate Std. Error    t value     Pr(>|t|)
## (Intercept)  0.07529289 0.05863517  1.2840910 2.011723e-01
## x           -0.04845372 0.12324295 -0.3931561 6.947856e-01
## m            0.49102547 0.07424300  6.6137609 6.835023e-10
## c1           0.35649550 0.10055884  3.5451432 5.297073e-04
## c2           0.39564302 0.07470576  5.2960174 4.336211e-07
## c3           0.12546383 0.05627968  2.2292920 2.734301e-02
```

More complex example VIII

- Model selection algorithms do not perform well
- They assume the covariates are either independent predictors or confounders
- Backwards selection

```
library(MASS)
```

```
##
## Attaching package: 'MASS'

## The following object is masked from 'package:dplyr':
##
##     select
```

```
stepAIC(fullmodel, direction = "backward", scope = list(lower = modelx),
        trace = 0)
```

More complex example IX

```
##
## Call:
## lm(formula = y ~ x + m + c1 + c2 + c3)
##
## Coefficients:
## (Intercept)            x            m           c1           c2
##     0.07529     -0.04845      0.49103      0.35650      0.39564
##          c3
##     0.12546
```

More complex example X

- Forwards selection

```
fwd <- step(modelx, scope = list(lower = modelx, upper = fullmodel),
            direction = "forward", trace = 0)
coef(fwd)
```

```
## (Intercept)           x          c2           m          c1          c3
##  0.07529289 -0.04845372  0.39564302  0.49102547  0.35649550  0.12546383
```

More complex example XI

- Both directions selection

```
bth <- step(modelx, scope = list(lower = modelx, upper = fullmodel),
            direction = "both", trace = 0)
bth$coefficients
```

```
## (Intercept)           x          c2           m          c1          c3
##  0.07529289 -0.04845372  0.39564302  0.49102547  0.35649550  0.12546383
```

- Pearl's Simpsons Machine example http://www.dagitty.net/learn/simpson/index.html
  - Stepwise inclusion of covariates changes the sign of the effect at every step

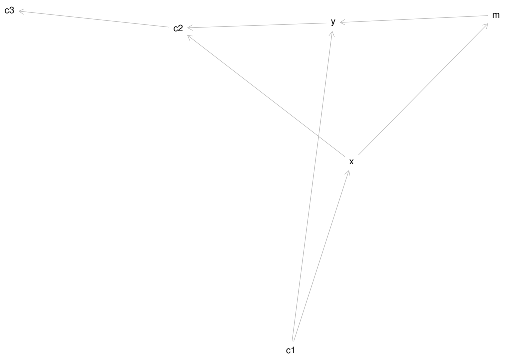
More complex example XII

- We can use `DAGitty` http://www.dagitty.net/ to help us (Textor et al. (2016))

```
library(dagitty)
complexg <- dagitty("dag {
                    x -> m -> y
                    x <- c1 -> y
                    x -> c2
                    y -> c2
                    c2 -> c3
            }")
```

More complex example XIII

```
plot(graphLayout(complexg))
```



More complex example XIV

- List testable implications

```
impliedConditionalIndependencies(complexg) %>% print()
```

```
## c1 _||_ c2 | x, y
## c1 _||_ c3 | c2
## c1 _||_ c3 | x, y
## c1 _||_ m | x
## c2 _||_ m | x, y
## c3 _||_ m | x, y
## c3 _||_ m | c2
## c3 _||_ x | c2
## c3 _||_ y | c2
## x _||_ y | c1, m
```

More complex example XV

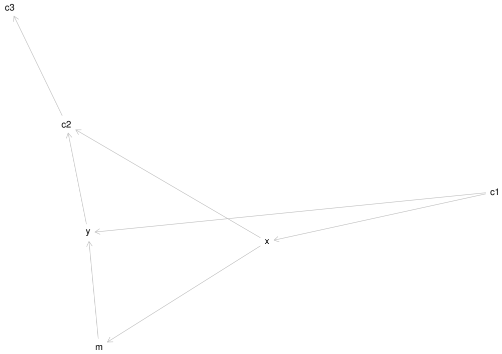
- Equivalence class
- Two DAGs are Markov equivalent if they represent the same conditional independence relations

```
eqdags <- equivalentDAGs(complexg)
length(eqdags)
```

```
## [1] 3
```

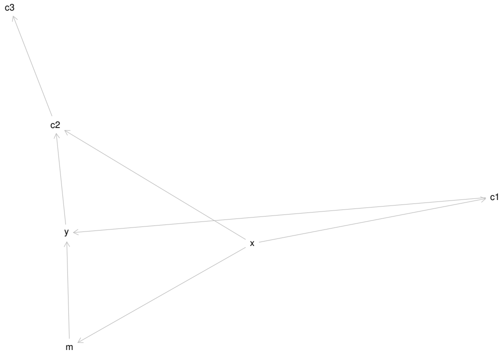
More complex example XVI

```r
plot(graphLayout(eqdags[[1]]))
```



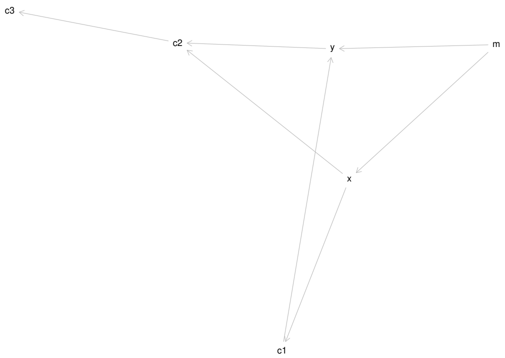
More complex example XVII

```r
plot(graphLayout(eqdags[[2]]))
```



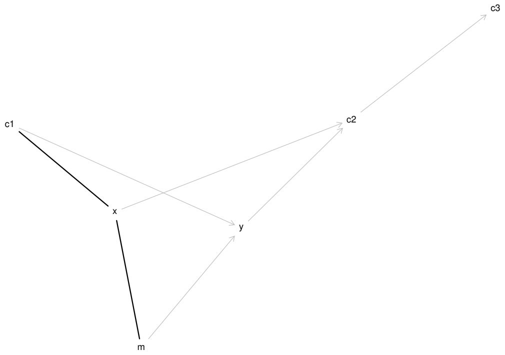
More complex example XVIII

```r
plot(graphLayout(eqdags[[3]]))
```



More complex example XIX

```r
eqclass <- equivalenceClass(complexg)
plot(graphLayout(eqclass))
```



More complex example XX

- Number of edges that can be reversed without changing the equivalence class

```
sum(edges(equivalenceClass(complexg))$e == "--")
```

```
## [1] 2
```

More complex example XXI

- List adjustment sets for effect of interest

```
adjustmentSets(complexg, "x", "y", effect = "direct" ) %>% print()
```

```
## { c1, m }
```

- List adjustment sets for total effect

```
adjustmentSets(complexg, "x", "y") %>% print()
```

```
## { c1 }
```

More complex example XXII

```
for(n in names(complexg)){
    for( m in setdiff(descendants(complexg, n ), n)){
        a <- adjustmentSets(complexg, n, m)
        if(length(a) > 0 ){
            cat("The total effect of ",n," on ",m,
                " is identifiable controlling for:\n", sep = "")
            print(a, prefix=" * ")
        }
    }
}
```

```
## The total effect of c1 on y is identifiable controlling for:
##  *  {}
## The total effect of c1 on c2 is identifiable controlling for:
##  *  {}
## The total effect of c1 on c3 is identifiable controlling for:
##  *  {}
## The total effect of c1 on x is identifiable controlling for:
##  *  {}
## The total effect of c1 on m is identifiable controlling for:
##  *  {}
## The total effect of c2 on c3 is identifiable controlling for:
##  *  {}
## The total effect of m on y is identifiable controlling for:
##  *  { c1 }
##  *  { x }
```

More complex example XXIII

```
## The total effect of m on c2 is identifiable controlling for:
##  *  { x }
## The total effect of m on c3 is identifiable controlling for:
##  *  { x }
## The total effect of x on m is identifiable controlling for:
##  *  {}
## The total effect of x on y is identifiable controlling for:
##  *  { c1 }
## The total effect of x on c2 is identifiable controlling for:
##  *  { c1 }
## The total effect of x on c3 is identifiable controlling for:
##  *  { c1 }
## The total effect of y on c2 is identifiable controlling for:
##  *  { x }
##  *  { c1, m }
## The total effect of y on c3 is identifiable controlling for:
##  *  { x }
##  *  { c1, m }
```

More complex example XXIV

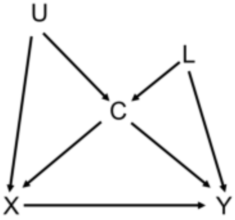
DAGitty's missing feature

- Pass it correlations between a set of variables (correlations) and generate all possible DAGs
  - Apparently this is being developed

Disadvantages of DAGs I

- They do not tell us the functional form of the model
  - What outcome model do we fit, e.g. linear regression/logistic regression etc.?
  - What parametric form should our variables have, e.g. X, X^2
- If there is confounding bias – we don't know if important
- If there is colliding bias – we don't know if important

Disadvantages of DAGs II



- We may even need to trade-off confounding and colliding biases:
  - If U and L both unmeasured
  - Not adjusting for C – confounding bias
  - Adjusting for C – colliding bias
  - We don't know which is worse without doing simulations for our example

Disadvantages of DAGs III

- If we decompose our effect with a mediator we don't know relative sizes of direct and indirect effects
- Difficult to represent interactions on a DAG
- Most realistically complex modelling situations will probably generate multiple plausible DAGs

Discussion

- Modelling guidelines informed by causal DAGs
    - Adjust for a set of variables sufficient to block all backdoor pathways between the two variables of interest
    - Do not adjust for colliders or variables caused by colliders
    - If a variable is on the causal pathway adjusting for it will decompose the effect of interest
- Thanks for your attention
- Any questions

References I

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