Predictor Selection

February 16, 2016

Biostatistics 208

Predictor Selection

- Define three primary goals in selecting predictors for regression models
- Application of DAGs in selecting confounders
- Applications of model selection algorithms

Predictor Selection

- Given a (potentially large) number of available predictors, which ones should be included in a regression model?
- Depends on "inferential goal":
  1. predict future outcomes
  2. estimate causal effect of a primary predictor
  3. identify important risk factors for an outcome
- Controversial, with positions dogmatically held

Goal 1: Prediction

- Includes diagnosis and prognostic risk stratification
- Often used in making decisions at the level of the individual
- Causal relationships useful, but not the primary focus
- Only strong predictors useful: (e.g. OR for binary diagnostic variable with sensitivity and specificity of 90% is 81)
- Model validation based on assessment of prediction error (PE)

Prediction Error

- Prediction error measures how well a model predicts a new outcome – i.e., for new observations not used in fitting model
- Two aspects of PE:
  1. *discrimination*: how well does model distinguish outcomes between individuals (e.g. cases from controls, high-risk patients from low, early from late events)?
  2. *calibration*: how accurately does model estimate outcomes, failure rates?
- Both discrimination and calibration are important

Prediction

- Bias-variance tradeoff and over-fitting
- Parameter estimates, predicted values:
  - biased when important predictors omitted from model
  - noisier when unimportant predictors are included
- Too many predictors results in fitting idiosyncrasies in the current data – i.e., over-fitting
- However, some methods for eliminating weak predictors can also cause trouble

Prediction: "traditional" split-sample approach

- *Example*: prediction of bone min. density (BMD) in subsample ($n \approx 2600$) from the Study of Osteoporotic Fractures (SOF)
- Model developed in 1/2 of the sample; validated in the remaining 1/2
- Model based on baseline predictors, selected using stepwise selection

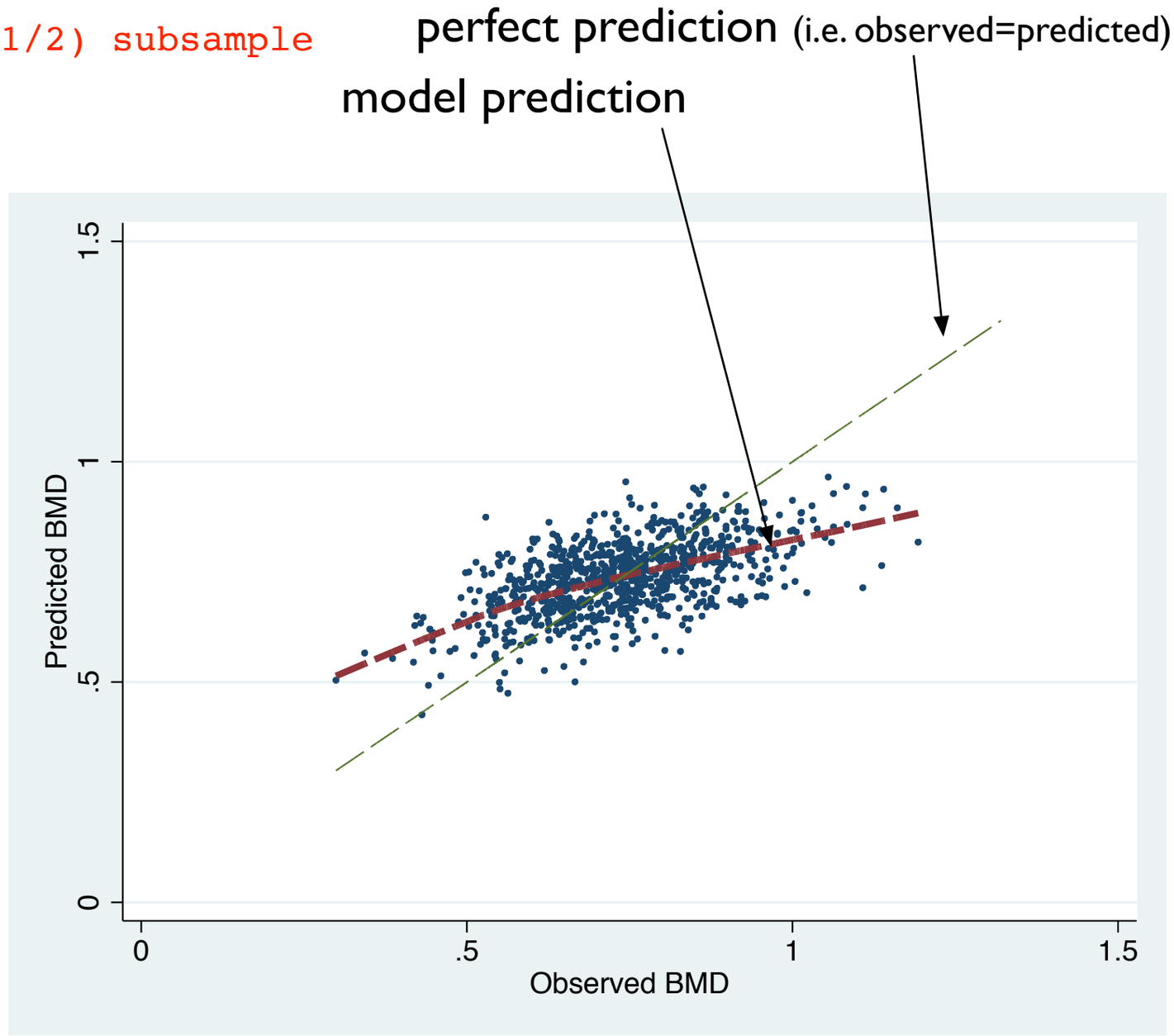
```
. * randomly order observations
. gen r = uniform()
. sort r
. * split sample into two groups consisting of 1/2, 1/2 of observations,
. * generate group indicator
. gen group = 1 if _n <= _N*0.5
(945 missing values generated)
. replace group=2 if group!=1
(945 real changes made)
. * results
. tabulate group, summarize(bmd)
            |           Summary of BMD
      group |        Mean   Std. Dev.       Freq.
------------+------------------------------------
          1 |   .73139813   .13575511        1389
          2 |   .72966763   .13541578        1390
------------+------------------------------------
      Total |   .73053257   .13556385        2779
```

Example prediction model from SOF

```
. * use backwards stepwise selection to select model, restricted to 1/2 of sample

. xi: stepwise, pr(.1): regress bmd eeu age lweight i.estrogen calsupp diuretic etid momhip usearms
(i.tandstnd) has10 gs10 gaitspd poorhlth caffeine drnkspwk smoker if group==1

      Source |       SS       df       MS              Number of obs =    1278
-------------+------------------------------           F( 13,  1264) =   52.89
       Model |  8.14515465    13  .626550358           Prob > F      =  0.0000
    Residual |  14.9745495  1264  .011846954           R-squared     =  0.3523
-------------+------------------------------           Adj R-squared =  0.3456
       Total |  23.1197041  1277  .018104702           Root MSE      =  .10884

------------------------------------------------------------------------------
         bmd |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    caffeine |  -.0396394     .01159    -3.42   0.001    -.0623772   -.0169017
         age |  -.0028671    .000776    -3.69   0.000    -.0043895   -.0013447
     lweight |   .8253971   .0396535    20.82   0.000     .7476031    .9031911
_Iestrogen_1 |   .0180801   .0070925     2.55   0.011     .0041657    .0319946
_Iestrogen_2 |   .0706062   .0086327     8.18   0.000     .0536702    .0875423
     calsupp |  -.0144882   .0066203    -2.19   0.029    -.0274763   -.0015002
    drnkspwk |   .0034561    .001295     2.67   0.008     .0009156    .0059967
        etid |  -.0674801   .0275688    -2.45   0.015    -.1215658   -.0133943
      smoker |  -.0313772   .0157915    -1.99   0.047    -.0623576   -.0003968
     usearms |  -.0519449   .0119332    -4.35   0.000    -.0753559   -.0285338
_Itandstnd_2 |  -.0159852   .0066144    -2.42   0.016    -.0289615   -.0030089
_Itandstnd_3 |  -.0193925   .0156356    -1.24   0.215    -.0500671    .0112821
_Itandstnd_4 |  -.0744849   .0394209    -1.89   0.059    -.1518225    .0028526
       _cons |  -.5337911   .1052804    -5.07   0.000    -.7403346   -.3272477
------------------------------------------------------------------------------
```

Example prediction model from SOF

```
. * Predict outcomes for validation (1/2) subsample
. predict pr if group==2
(option xb assumed; fitted values)
(1454 missing values generated)
. * Estimate R^2 for validation group
. * (to assess discrimination)
. corr bmd pr
(obs=1325)
             |      bmd       pr
-------------+------------------
         bmd |   1.0000
          pr |   0.5639   1.0000
. display r(rho)^2
.31802397
* Plot observed vs predicted values
. * (to assess calibration)
. twoway (scatter bmd pr, msize(vsmall)) (lowess bmd pr, sort lpattern(longdash)
lwidth(thick)), ytitle("Predicted BMD") xtitle("Observed BMD") legend(off)
```



Potential problems with example approach

- Fitting procedure:
  - doesn't account for interaction & nonlinearity
  - backwards selection ignores many models
  - criteria for predictor selection limited to estimation sample, based on observed associations with outcome (i.e. overfitting a possibility)
- Validation assessment:
  - choice of 1/2, 1/2 split arbitrary (potentially inefficient)
  - single split provides limited assessment of PE
  - validation applies to study pop.
- Available predictors do not adequately support outcome predictions

Model selection strategies to avoid over-fitting

1. Pre-specify well-motivated predictors, how to model them
2. Eliminate predictors without using the outcome
3. Select model to minimize "optimism"-corrected PE measure
4. "Shrink" coefficient estimates for poor performing predictors (e.g. "LASSO" regression methods)

Selection to minimize optimism-corrected PE

- Naïve methods – e.g., selecting model to maximize R^2 in training data – lead to over-fitting, optimistic estimates of clinical utility
- Use of an optimism-corrected measure of PE helps avoid over-fitting
- External validation also needed (Altman & Royston, What do we mean by validating a prognostic model? *Stat Med*, 2000;19:453-73)

Optimism-corrected estimates of PE

- Naïve measures penalized for number of predictors: adjusted R^2, AIC, BIC (`estat ic` postestimation command in Stata)
- Use different data to estimate parameters, evaluate PE
  - split-samples (as in SOF example)
  - h-fold cross-validation
  - bootstrap

Optimism-corrected PE: h-fold cross-validation

- Divide data into h = 5 to 10 subsets, then for each subset:
  - fit model to the remaining subsets combined
  - obtain predictions for excluded subset
- Calculated PE from complete set of predictions; repeat
- Do this for each candidate model, select model with minimum cross-validated PE
- More efficient than single split-sample or leave-one-out methods

Example: 2-fold cross-validation for SOF example

- Downloadable Stata utility `regvalidate` uses two-fold cross-validation

```
. quietly xi: stepwise, pr(.1): regress bmd eeu age lweight i.estrogen calsupp diuretic
etid momhip usearms (i.tandstnd) has10 gs10 gaitspd poorhlth caffeine drnkspwk smoker

. regvalidate, reps(50)

original sample size = 2542   reps = 50

regression model: stepwise , pr(.1): regress bmd eeu age lweight _Iestrogen_* calsupp
diuretic etid momhip usearms (_Itandstnd> _*) has10 gs10 gaitspd poorhlth caffeine
drnkspwk smoker

                orig          train          test          diff          orig adj
R-squared       0.3475        0.3506         0.3339         0.0167        0.3309
rss/n           0.0118        0.0119         0.0121        -0.0002        0.0120
fit slope       0.9925        0.9936         0.9668         0.0268        0.9657
fit _cons       0.0064        0.0051         0.0252        -0.0200        0.0264
```

- adjusted estimates are optimism-corrected (compared to original estimates)
- in general, 5-10 fold cross validation is preferable

Optimism-corrected PE: bootstrapping

- In each of, say, 200 bootstrap samples
  - fit model to bootstrap sample, obtain predictions
  - evaluate PE in bootstrap, original samples
  - average difference in paired PEs estimates optimism
- Fit model to original data, calculate naïve PE, penalize by average bootstrap optimism
- Do this for each candidate model, select model with minimum penalized PE

Application: Point score prediction models

- Individual outcome predictions from model-based risk scores
- Points derived by rounding model coefficients
- Motivation is clinical utility
- Examples: TIMI (Thrombolysis In Myocardial Infarction), versions of Framingham
- Discrimination, calibration can suffer (Gordon et al. Coronary risk assessment by point-based and equation-based Framingham models: significant implications for clinical care. Journal of General Internal Medicine. 2010)

Recommendations for Goal 1

- For clinical use, select easily available predictors
- Pay attention to nonlinearity and interactions in fitting candidate models
- To avoid over-fitting:
  - eliminate candidate predictors without using outcome
  - select model using cross-validation or bootstrap
- Check loss of discrimination, calibration before going to point score models
- Validate model in external test set
- Consider applying modern *machine learning* tools (e.g. random forests, super learner) in applications where number of predictors and interpretability are not of primary concern

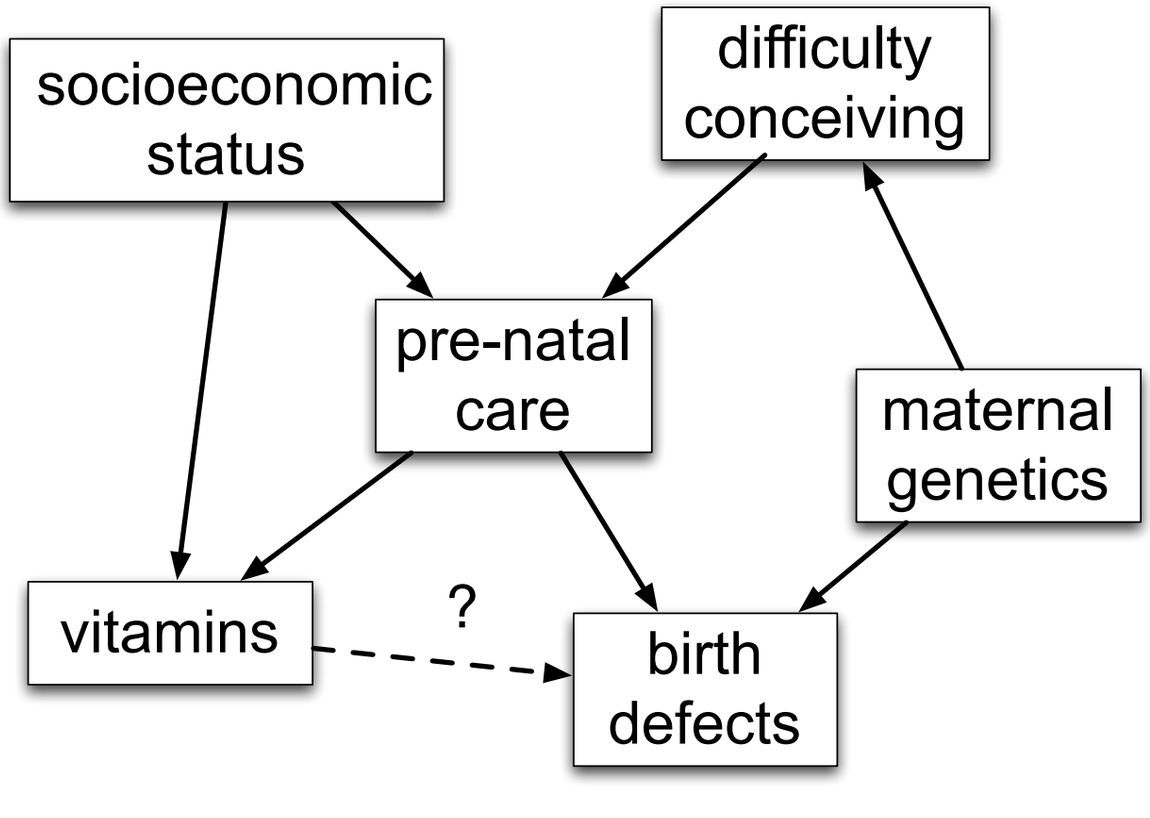
Goal 2: Assessing a predictor of primary interest

- Research question focuses on a single predictor
  - *Example*: Does maternal vitamin use reduce risk of birth defects?
- Ruling out confounding is key
- Minimizing PE is not critical, so over-fitting not a central issue
- Directed acyclic graphs (DAGs) central in model selection for this goal

Directed Acyclic Graphs (DAGs)

- Help identify what we do and *do not* need to control for to avoid confounding
- Primary predictor, outcome, potential confounders and mediators represented as *nodes* of the DAG
- Causal relationships depicted as *directed edges*
- No factor can cause itself, hence graph is *acyclic*
- A useful DAG requires *a lot* of prior substantive information about what causes what – and what doesn't

Maternal vitamin use and birth defects

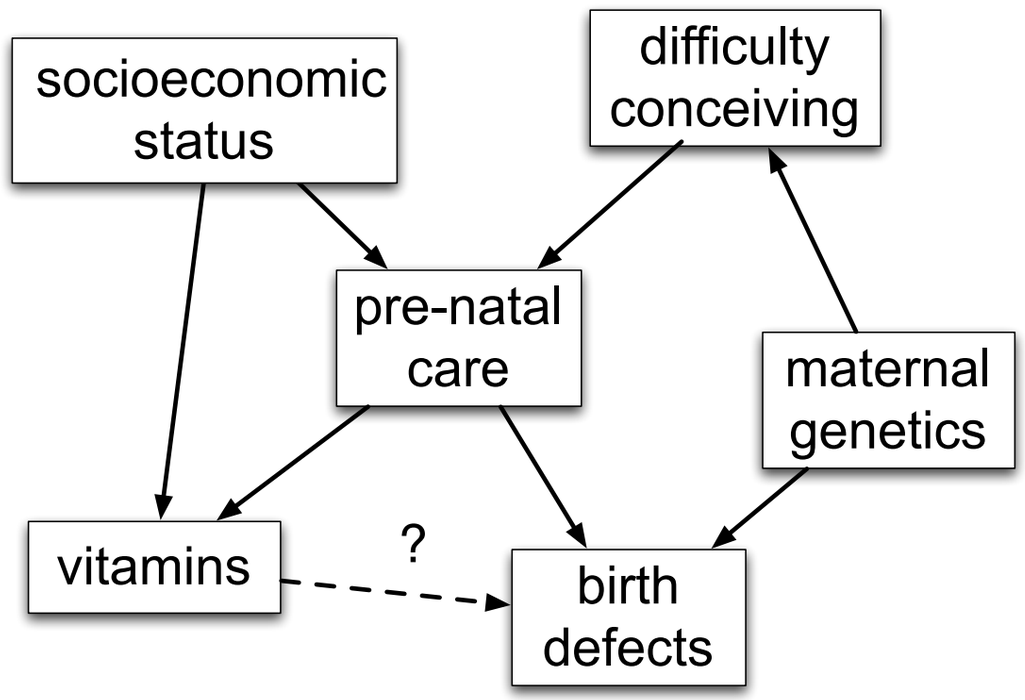


Assumptions about causal pathways:

- Prenatal care (PNC) increases vitamin use, and reduces risk of birth defects directly
- Difficulty conceiving may lead mother to seek PNC
- Maternal genetics affects birth defects and also difficulty conceiving
- SES affects both access to PNC and vitamin use

Additional assumptions in this DAG

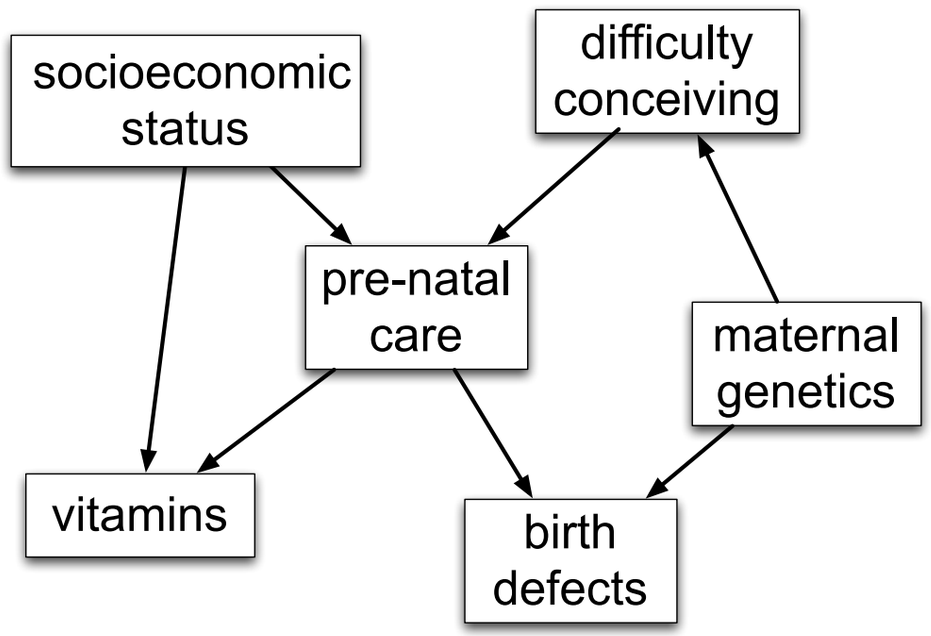
- SES affects birth defects only via PNC, vitamin use
- Difficulty conceiving affects vitamin use only through PNC
- No other common causes of vitamin use and birth defects
- In summary, no excluded confounders or directed edges



Backdoor paths

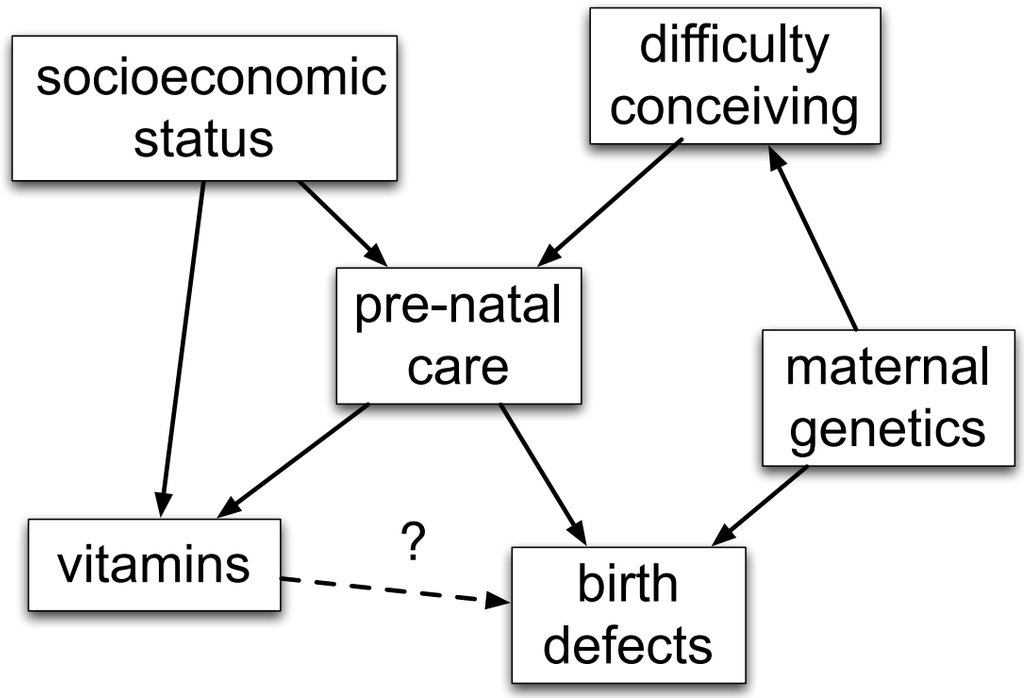
- After removing directed edge from vitamin use to birth defects, four backdoor paths remain between them:

1. Vitamin use ← pre-natal care → birth defects
2. Vitamin use ← SES → pre-natal care → birth defects
3. Vitamin use ← pre-natal care ← difficulty conceiving ← maternal genetics → birth defects
4. Vitamin use ← SES → pre-natal care ← difficulty conceiving ← maternal genetics → birth defects



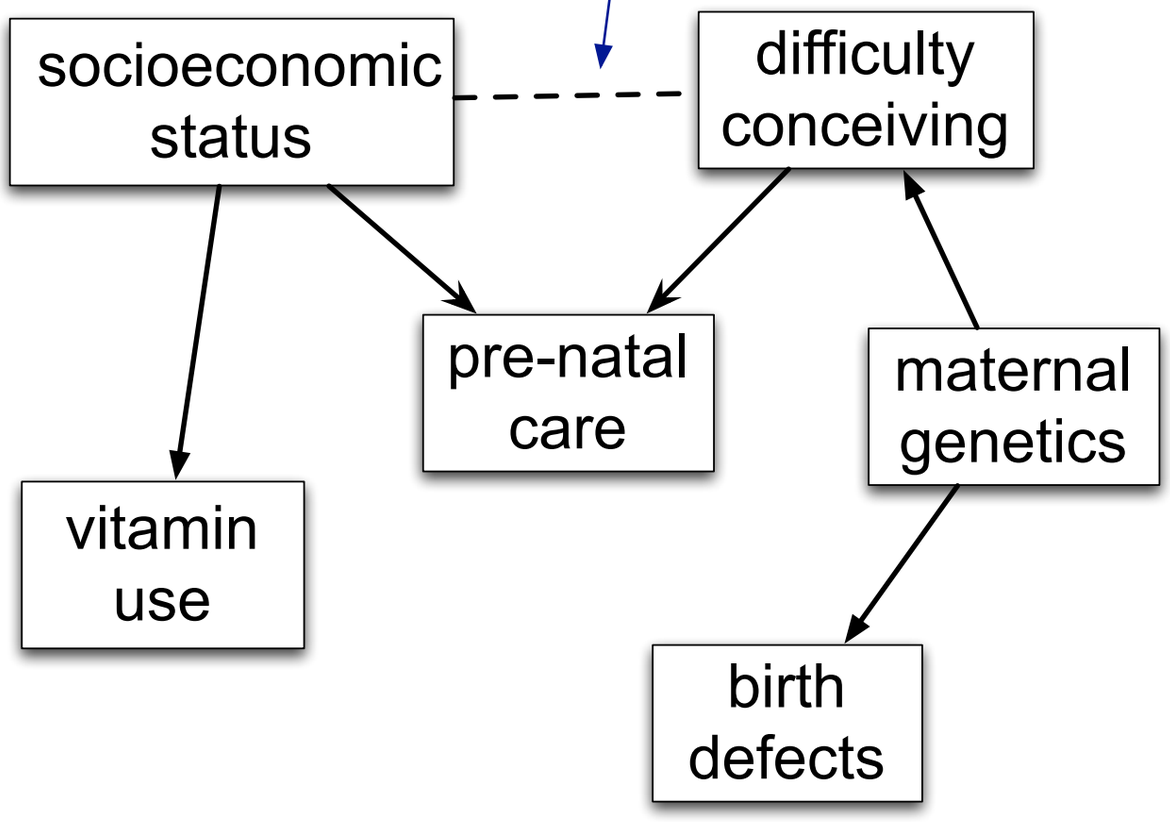
Colliders

- A *collider* on a backdoor path between exposure and outcome is a node with incoming arrows from both directions
- Pre-natal care is a collider of the fourth backdoor path
- It is not a collider on any other backdoor path
- Controlling for pre-natal care would induce a correlation between its common causes, SES and difficulty conceiving, opening a fifth backdoor path



Controlling for a collider induces an association

- Controlling for PNC is tantamount to stratifying on it
- Within PNC user stratum:
  - SES, difficulty conceiving competing explanations for PNC
  - higher SES women less likely to have had difficulty conceiving, and vice versa
- Controlling for PNC opens a backdoor path (representing a negative correlation) via induced association of SES and difficulty conceiving

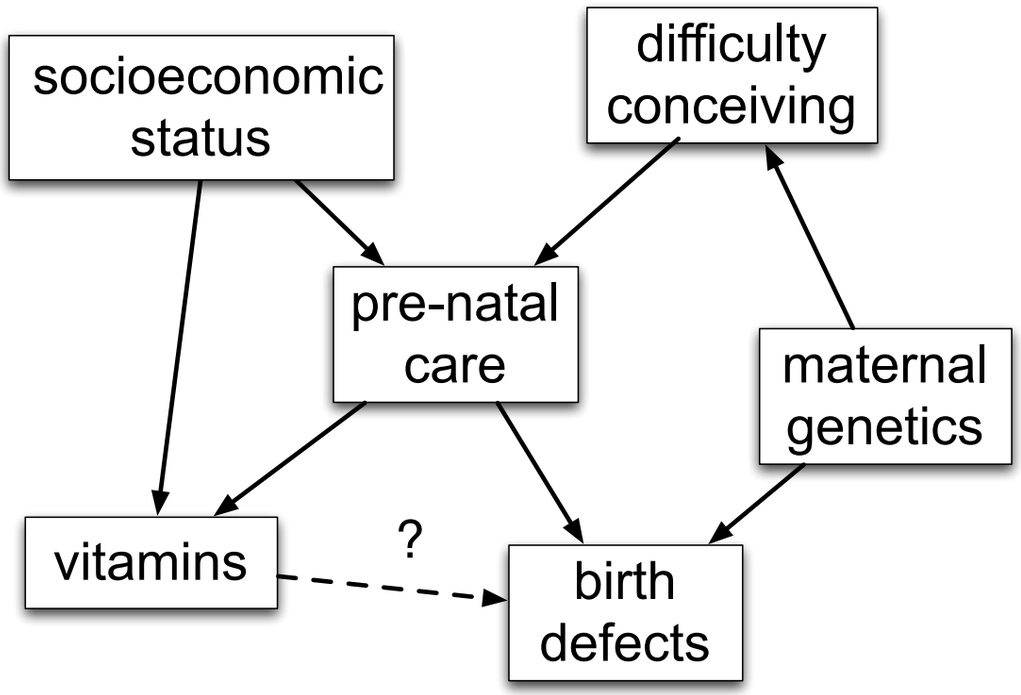


Open and blocked backdoor paths

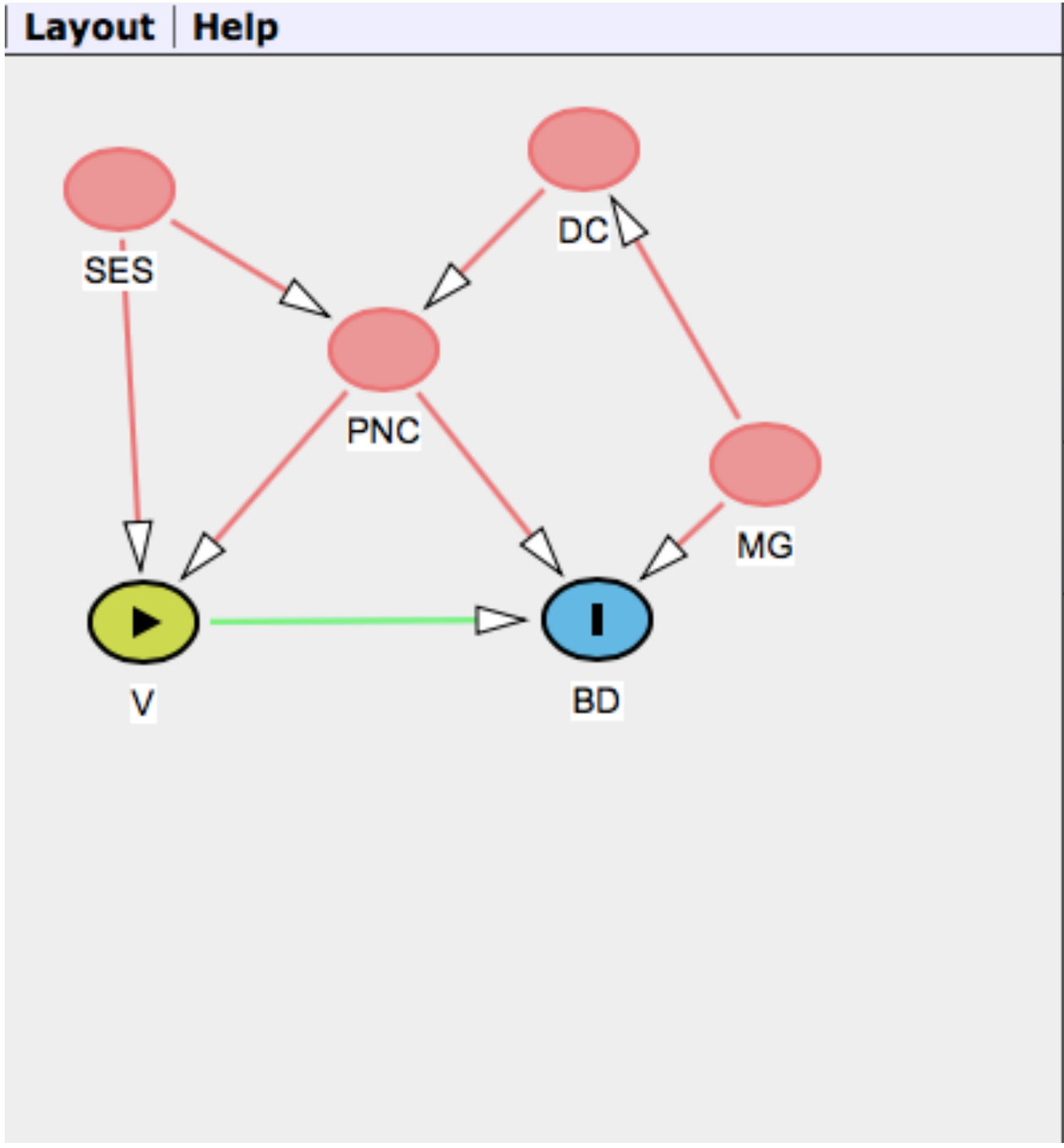
- If any of the backdoor paths between vitamin use and birth defects remains open, we would expect to find an association between them, even if there was no causal effect
- A backdoor path is blocked, provided we control for at least one non-collider on the path.
- A backdoor path including a collider is blocked provided we do *not* control for the collider
- If we do control for the collider, we need to control for a non-collider on the backdoor path to block it

What do we need to control for?

- Controlling for pre-natal care blocks the first three backdoor paths, but it is also a collider
- Controlling for it opens the fourth backdoor path, but controlling for any non-collider on that path will block it
- Controlling for SES or difficulty conceiving would be cheaper and easier than maternal genetics



Determination of MSAS using dagitty.net



Adjustment for total effect

Minimal sufficient adjustment sets for estimating the total effect of V on BD:

- {DC, PNC}
- {MG, PNC}
- {PNC, SES}

Adjustment for direct effect

Total and direct effects are equal in this model.

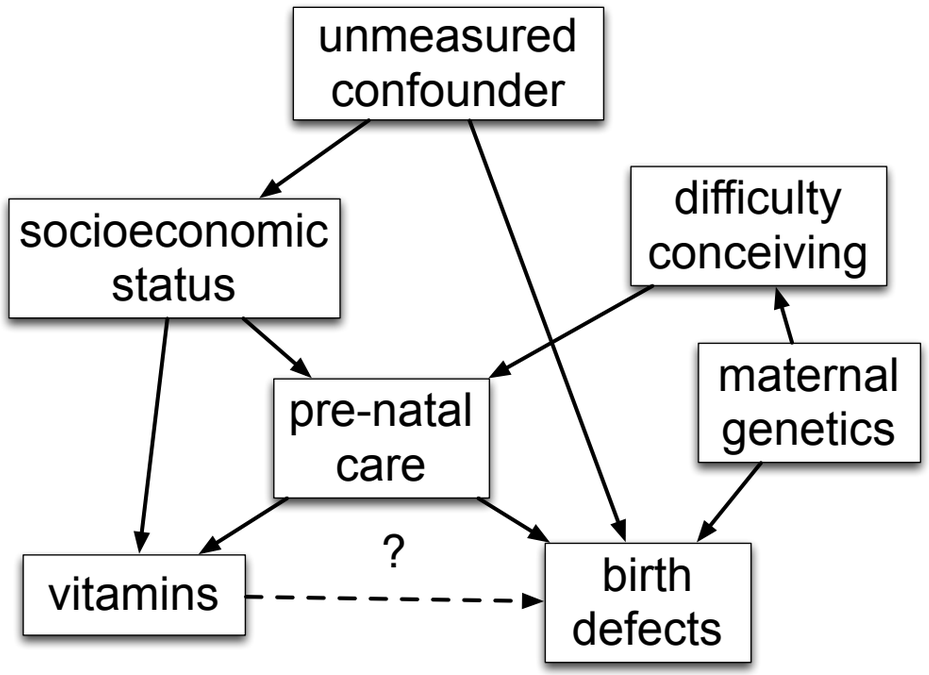
Testable implications

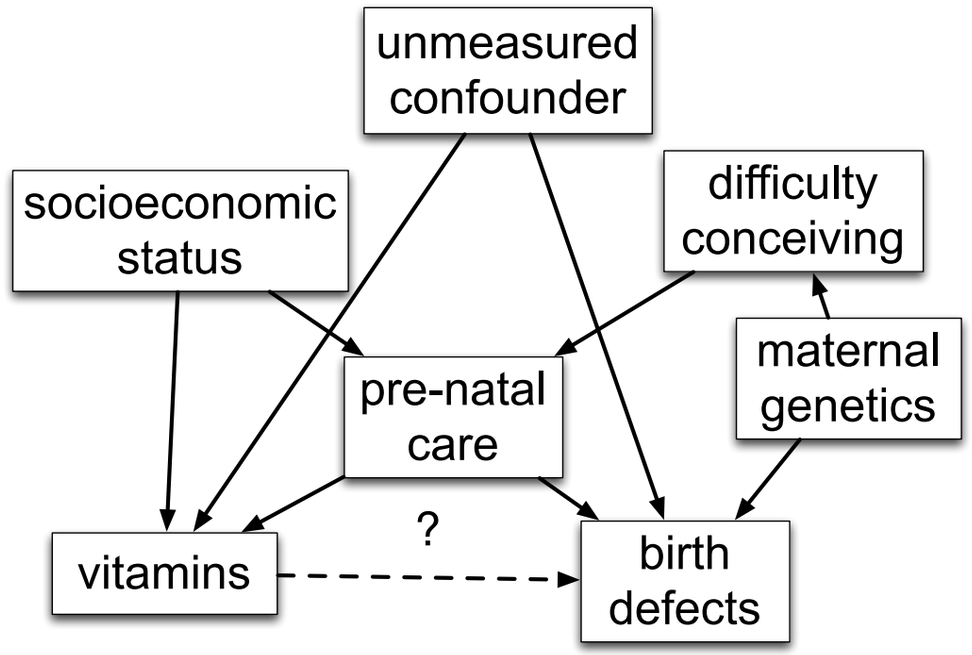
The model implies the following conditional independences:

- V ⊥ DC | PNC, SES
- V ⊥ MG | DC
- V ⊥ MG | PNC, SES
- BD ⊥ SES | DC, PNC, V
- BD ⊥ SES | MG, PNC, V
- BD ⊥ DC | MG, PNC, SES
- BD ⊥ DC | MG, PNC, V
- SES ⊥ DC
- SES ⊥ MG

Remaining issues to consider in confounding control

Unmeasured confounders

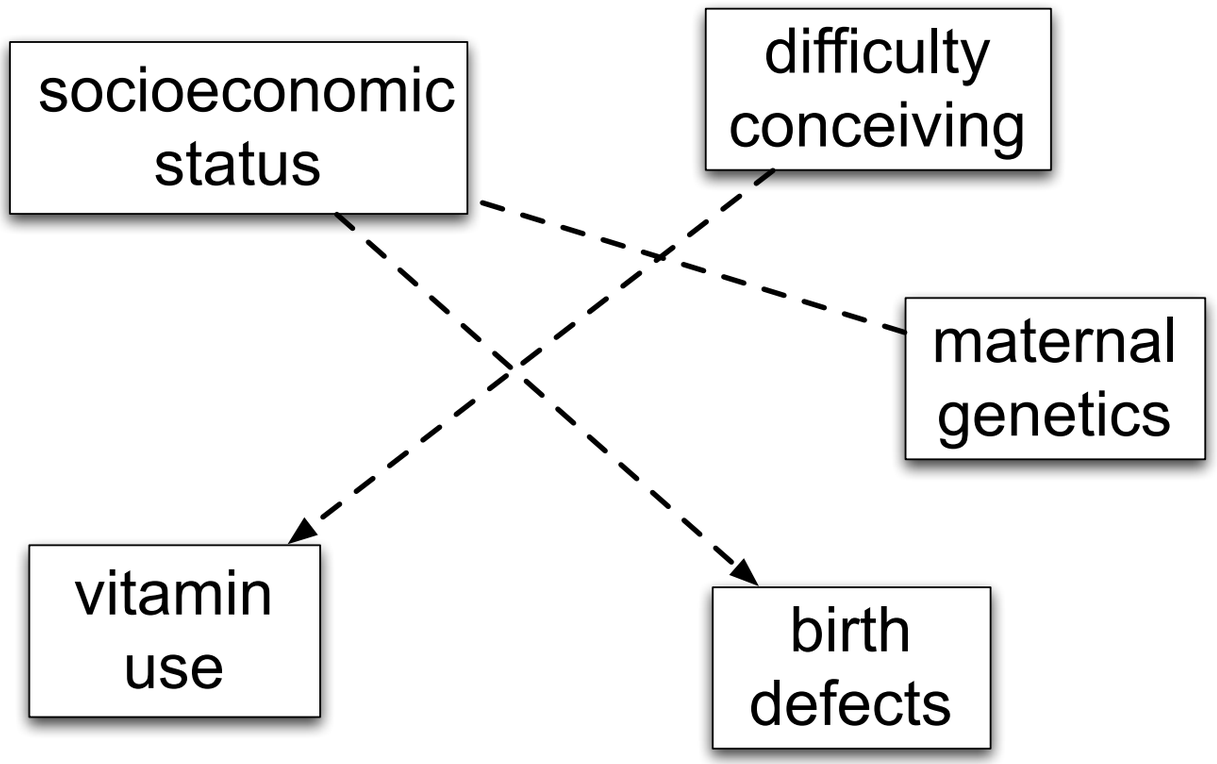




- DAGS can help determine vulnerability to unmeasured confounders
  - provided we have sufficient information about their effects
- Depends on what the measured confounder affects

Remaining issues to consider in confounding control

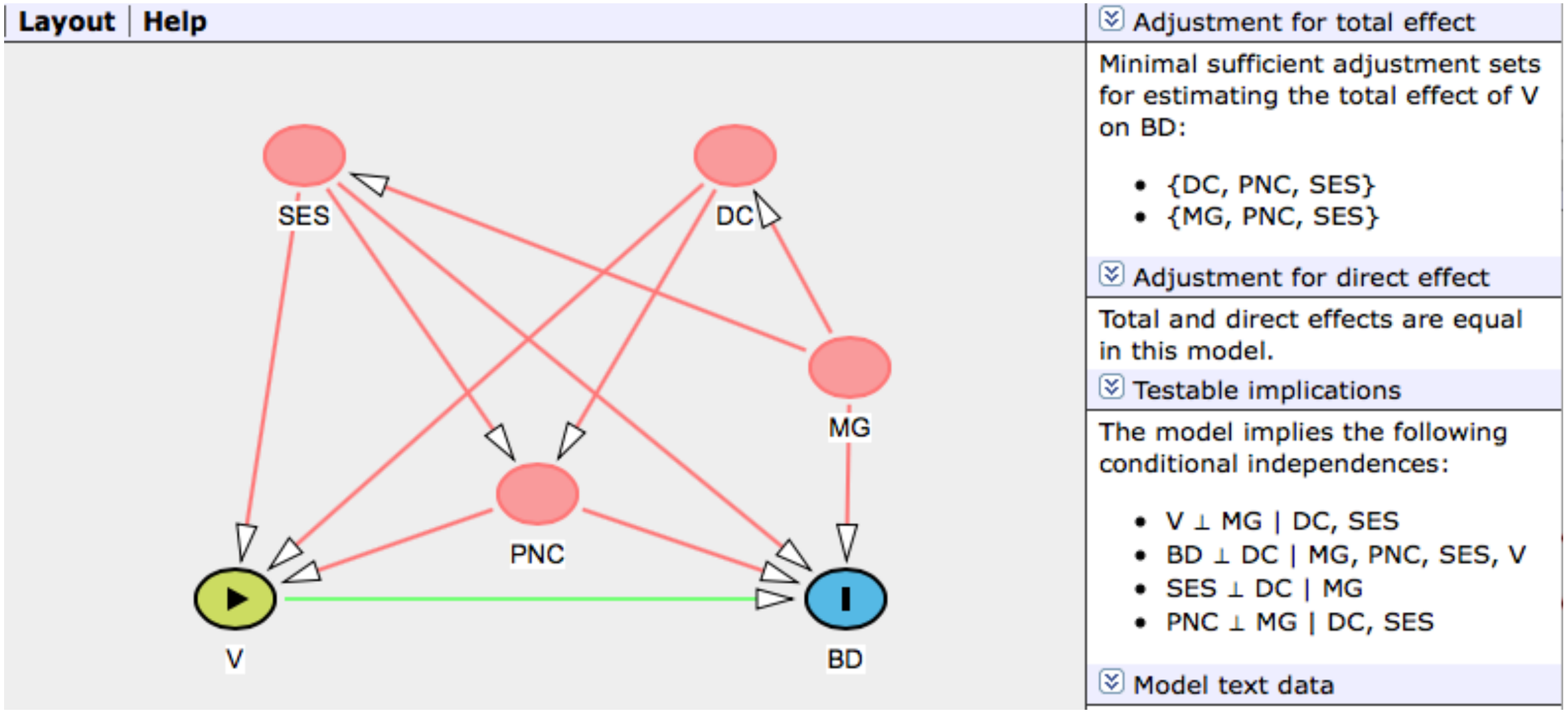
Other plausible causal pathways (edges) to consider:



- SES may affect birth defects via environmental exposures
- Discrimination may link maternal genetics and SES
- Difficulty conceiving could lead directly to vitamin use
- If all these paths are open, we would need to control for SES and difficulty conceiving or maternal genetics to block them
- (Succinct DAGs are not too hard to second guess)

Remaining issues to consider in confounding control

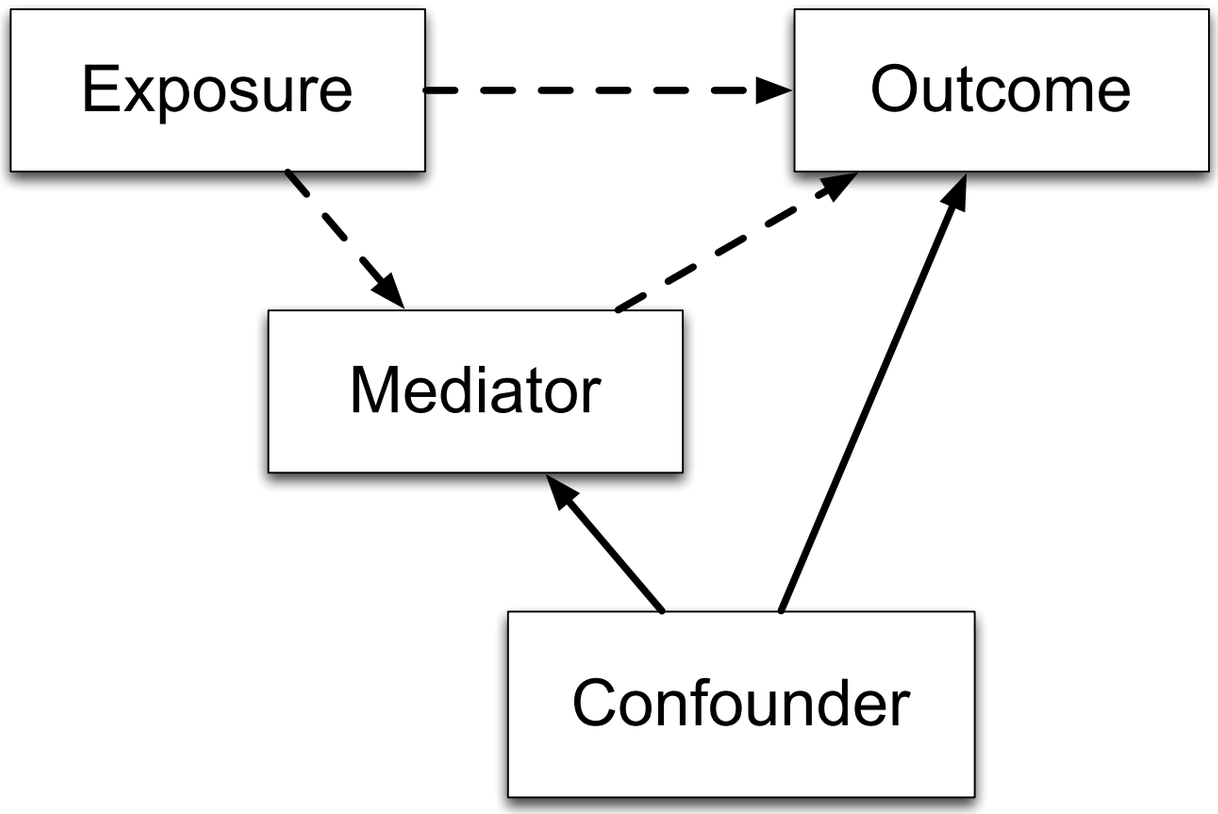
- MSAS options resulting from considering other plausible causal connections



Other insights from colliders

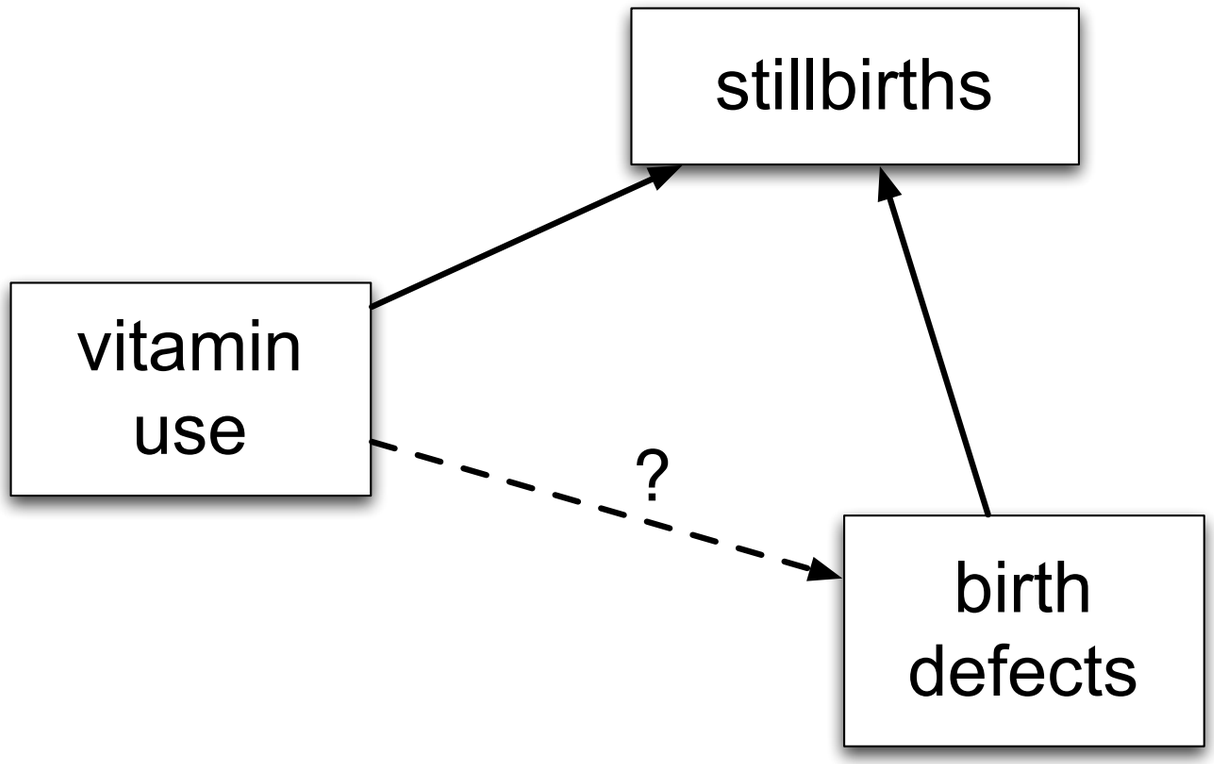
- Need to adjust for confounders of mediator/outcome relationship
- Don’t adjust for a common effect of exposure and outcome
- Don’t adjust for a common effect of unmeasured causes of exposure and outcome

Confounders of mediator/outcome relationship



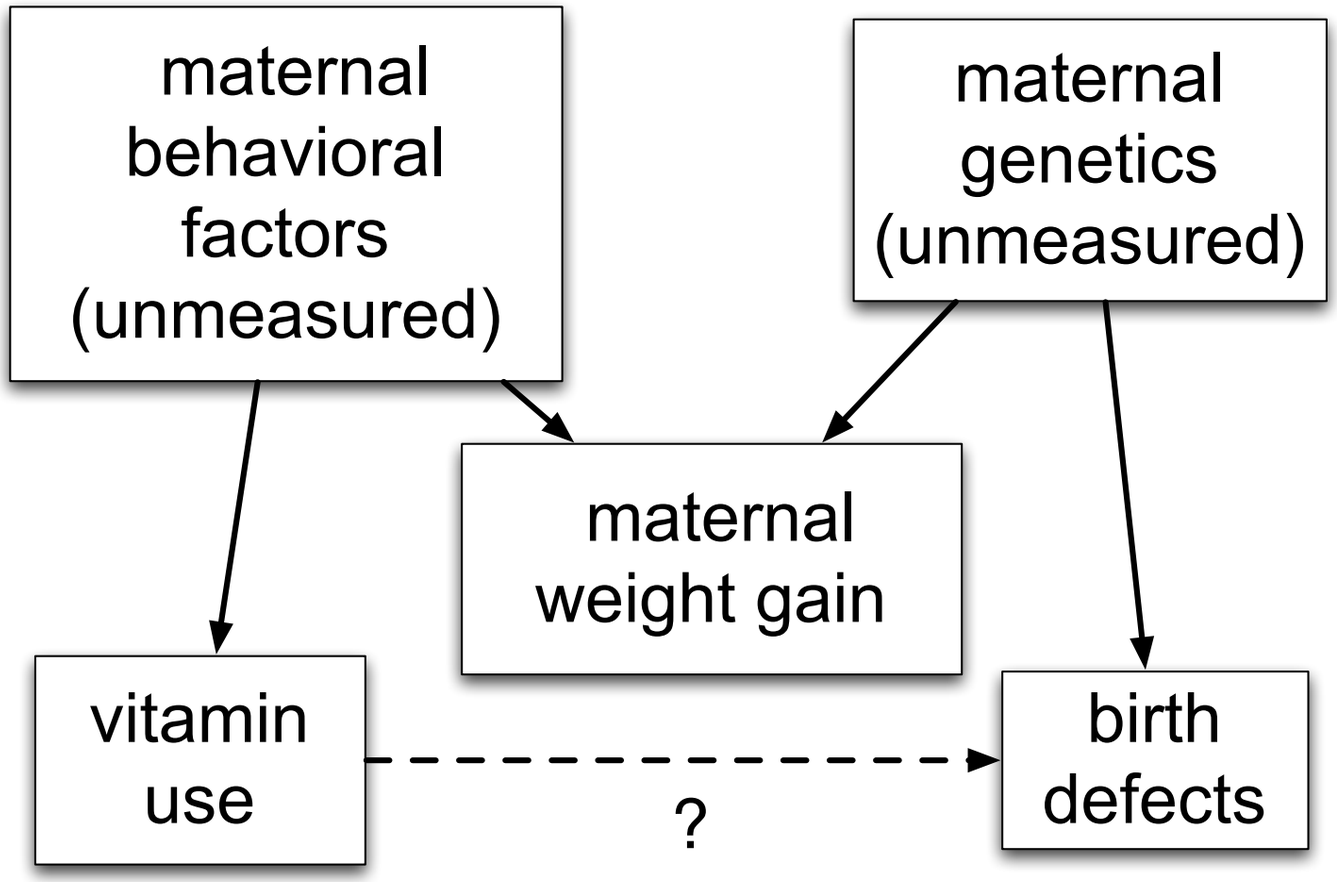
- If Mediator is a collider - stratification on Mediator will result in a spurious assoc. between Exp. & Out. (Cole SR, Hernán MA. Fallibility in estimating direct effects, Int J Epid, 2002;31:163-5)

Common effect of exposure, outcome



- Stillbirths a possible common effect of vit. use & birth def.

Common effect of unmeasured causes of outcome "M-colliders"



- *Note*: in the case that causal links are weak, potential bias from adjustment is likely small (can try adjusting/not as a sensitivity analysis)

Insights from DAGs

- Exclude from model:
  - mediators (unless estimating direct effect)
  - common effects of outcome and exposure
  - redundant confounders
- Adjusting for a confounder/collider (e.g., PNC) may require adjusting for additional factors
- Often > 1 minimum sufficient adjustment set (MSAS)

Weakly supported ("*B*-list") confounders

- Frequently there are "*B*-list" measured variables with weakly-supported confounding roles
- If DAGs including, excluding *B*-list confounders have a common MSAS, go with it
- Otherwise:
  - use most feasible MSAS based on DAG including *B*-list
  - sequentially drop *B*-list confounders if adjusted coefficient estimate for primary predictor changes < 5% or 10%
- If uncertainty about causal direction (i.e., possible M-collider) affects estimate for primary predictor by > 5% or 10%, report and discuss implications

Approach to dropping *B*-list confounders

- Suppose X_1 and X_2 are on *B*-list, and co-linear
- Whether each meets the change-in-coefficient criterion can depend on whether other is included
  - each can look unimportant if the other is included, important otherwise
- Requires a cyclical procedure like those used in Stata `stepwise (sw)` commands

Algorithm for dropping *B*-list confounders

- Starting from full model determined by MSAS including *B*-list
  1. Evaluate change-in-coefficient criterion for each confounder on *B*-list one at a time
  2. Drop the one with smallest change < 5% or 10%
  3. Repeat steps 1 and 2, starting from reduced model, until all remaining *B*-list confounders meet retention criterion

Algorithm for dropping *B*-list confounders

- Full *B*-list includes X_1, X_2, and X_3; X_1 and X_2 co-linear
- Iteration 1: dropping X_1 changes coefficient by 1%, dropping X_2 changes it by 2%, X_3 by 15% → drop X_1
- Iteration 2: dropping X_2 changes coefficient by 12%, X_3 by 17% → done
- This means fitting 5 extra models, calculating change-in-coefficient for primary predictor for each one
- We wrote Stata command to automate this procedure; introduced in lab

Limitations of DAGs

- No good way to represent interactions, no guidance about keeping or excluding them
- No representation of functional form (i.e., linearity)
- Co-linearity, allowable numbers of predictors ignored; more later about these issues
- Can be hard to specify convincingly

Recommendations for Goal 2

- Use DAG to identify MSASs, exclude mediators, common effects of exposure and outcome
  - use Dagitty.net for complicated DAGs
  - choose the most feasible MSAS
  - use change-in-estimate criterion, sensitivity analysis to deal with weakly supported potential confounders
- More later on number of predictors, interactions with main predictor, mediation, high correlation among confounders
- Alternative procedure when you can't draw a convincing DAG
  - identify an *A*-list of confounders strongly supported by the literature and/or face validity
  - identify a *B*-list of plausible but unclearly supported potential confounders
  - exclude mediators, common effects of exposure and outcome
  - use change-in-coefficient criterion to exclude unimportant *B*-list confounders

Recommendations for Goal 2 (*continued*)

- Hypothesis testing only of interest for primary predictor – so somewhat robust against inflation of type-I error
  - type-I errors for covariates are irrelevant
  - results for covariates can be left in the background
  - Over-fitting is primarily a problem for Goal 1, not Goal 2

Randomized Trials - a Special Case of Goal 2

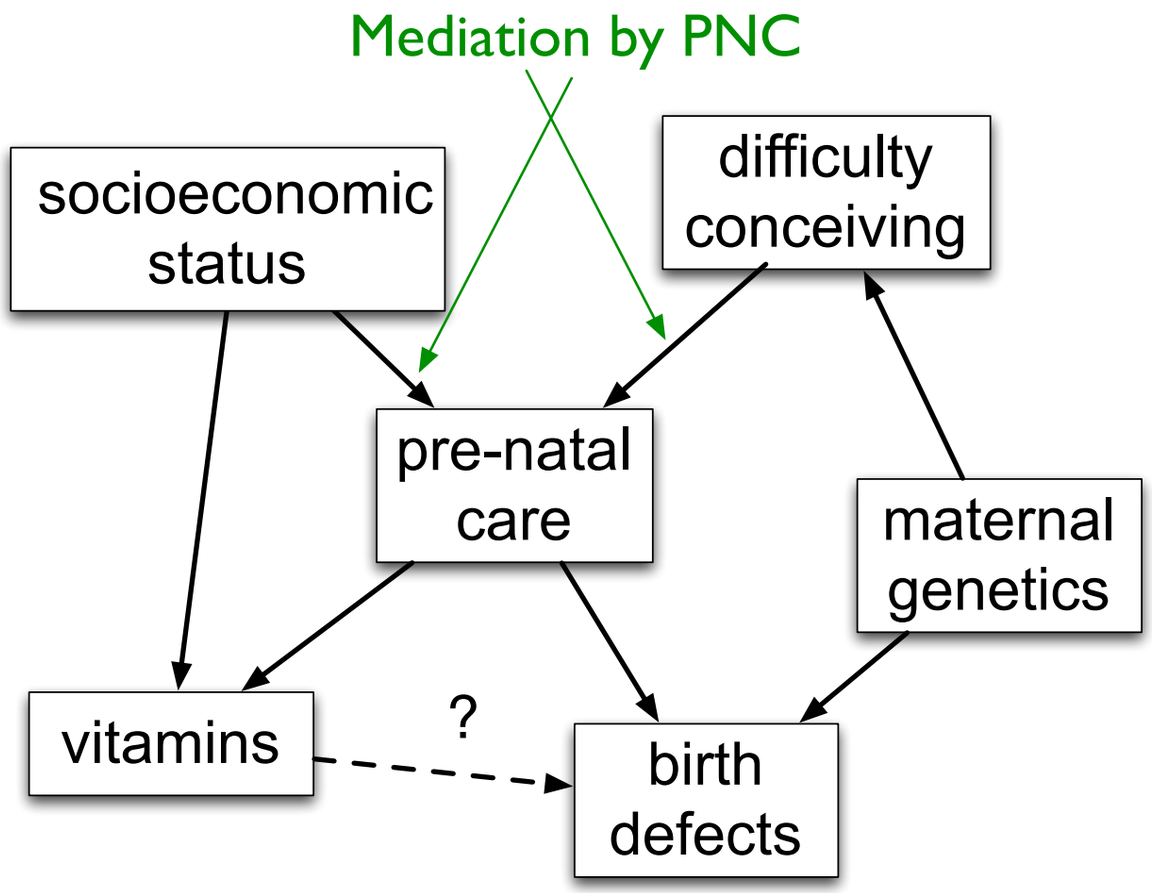
- Treatment the predictor of primary interest
- Confounding not an issue, provided randomization succeeds
- Include covariates to
  - account for clustering by clinical center
  - reduce variance using pre-specified stratification variables
- Do *not* adjust for any post-randomization variables

Goal 3: evaluating multiple predictors as risk factors for an outcome

- What are the risk factors for an outcome?
- Most difficult of three inferential goals
- Instead of one predictor of primary interest, several variables may be targeted

Goal 3: potential problems

- Many possible mediating, interaction relationships
- False positive findings, particularly for interactions
- No single model will summarize causal relationships
  - hard to achieve unconfoundedness for all included factors
  - mediation often an issue (e.g. in assessing effects of SS & DC in example below)



Recommendations for Goal 3

- Ruling out confounding is still central
- *Best* (but labor intensive) solution: treat each predictor as primary in turn, use DAG-based methods for Goal 2 (not the position taken in Section 10.3.2 of book)

An alternative approach

- Fit a single big model including potential confounders
  - needed for face validity, regardless of statistical criteria
  - if they meet liberal statistical inclusion criterion ($p < 0.2$)
    - *Note:* change-in-coefficient criterion not applicable (i.e. many coeff. involved)
- Cautiously interpret weaker, less plausible findings
- Multiple models may be required to deal with mediation

Additional topics in predictor selection

Techniques for selecting parsimonious models

- Retain only variables with $p < 0.05$ for goals 2 and 3?
- Motivations:
  - avoid over-fitting
  - Occam's razor: simpler explanations likelier – limit type-I errors
  - less to explain in the discussion
- Drawback: residual confounding, especially in small samples

Parsimonious models - over fitting

- Goal 1:
  - over-fitting increases prediction error
  - parsimonious models often have lower prediction error (predictors best chosen by cross-valid./bootstrap to minimize PE)
- Goal 2:
  - parsimony can lead to uncontrolled confounding
  - over-fitting of covariates usually not a problem

Number of predictors to include?

- Too many predictors can
  - degrade precision
  - in smaller datasets, swamp a real association
  - induce bias in some nonlinear models (e.g. logistic and Cox regression)

Recommendations: number of predictors

- Use 10-15 observations/predictor (10 events per predictor for binary/ survival outcomes) as a cautionary flag
- If you are close to 10, check for
  - high correlations between predictors
  - inflated SEs when a new covariate is added
  - inconsistency between Wald and likelihood ratio tests (logistic and Cox models)
  - gross inconsistency with smaller models
- If trouble is apparent:
  - tighten inclusion criterion to $p < 0.15$ or $p < 0.1$
  - omit variables included only for face validity
- With a binary primary predictor, many potential confounders, and a rare outcome, consider *propensity scores*
  - *Note:* propensity scores don't solve the problem with a rare predictor, or control for unmeasured confounders

Co-linearity between predictors

- Variance inflation factor (*VIF*): variability (SE) of β_j (coeff. for j^{th} predictor) increases with corr. (r_j) between x_j and other predictors in model (see lecture 2 & sect. 4.2.2.2):

$$VIF(\hat{\beta}_j) = \frac{1}{(1 - r_j^2)}$$

- Can make coefficient estimates very imprecise, even when F test for combined effects is statistically significant
- Co-linear predictors give similar information about outcome
  - p-values don't help distinguish between them

Diagnosing co-linearity

- High pairwise correlations (r) between predictors: caution if $r > 0.8$, trouble if $r > 0.9$
- Check variance inflation factors (`estat vif` postestimation command); watch out for *VIF* > 5
- If either of two co-linear predictors is included one at a time, *t*-test for predictor is significant
- In model with both predictors, *F*-test for joint effect significant, *t*-tests are not

Recommendations: dealing with co-linearity

- Goal 1: use cross-valid. to select one of co-linear predictors
- Goal 2: co-linearity between predictor of interest and a confounder in every MSAS: you may have to admit defeat
- Goal 3: see if the model solves the problem: e.g., one clearly dominates, or both are independently predictive. Or, if it makes sense, create summary variables or select among them
- Co-linearity between control variables (e.g. between confounders in goal 2, or between variables included in polynomial or spline terms): *not* a problem

Example co-linearity between control variables

- From lab 6: controlling for non-linearity in a continuous predictor by adding polynomial (e.g. squared) terms

```
* regression of BMD on age and weight (including square of weight)

. reg bmd age weight weight2

      Source |       SS       df       MS              Number of obs =     278
-------------+------------------------------           F(  3,   274) =   43.38
       Model |  1.67578732     3  .558595772            Prob > F      =  0.0000
    Residual |  3.52855652   274  .012877943            R-squared     =  0.3220
-------------+------------------------------           Adj R-squared =  0.3146
       Total |  5.20434383   277  .018788245            Root MSE      =  .11348

------------------------------------------------------------------------------
         bmd |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0047303   .0015033    -3.15   0.002    -.0076897   -.0017709
      weight |   .0182735   .0035289     5.18   0.000     .0113263    .0252207
     weight2 |  -.0000925   .0000239    -3.87   0.000    -.0001395   -.0000455
       _cons |   .3012021   .1826122     1.65   0.100    -.0582992    .6607034
------------------------------------------------------------------------------

. corr bmd weight weight2
             |      bmd   weight  weight2
-------------+---------------------------
         bmd |   1.0000
      weight |   0.5080   1.0000
     weight2 |   0.4742   0.9896   1.000

. estat vif
    Variable |       VIF       1/VIF
-------------+----------------------
      weight |     48.58    0.020585
     weight2 |     48.39    0.020665
         age |      1.07    0.938879
```

Example co-linearity between control variables

```
* regression of BMD on age and weight (including square of centered weight)

. quietly summ weight

. gen cweight2 = (weight - r(mean))^2

. corr weight weight2 cweight2
             |   weight  weight2 cweight2
-------------+---------------------------
      weight |   1.0000
     weight2 |   0.9896   1.0000
    cweight2 |   0.4528   0.5764   1.0000

. reg bmd age weight cweight2
      Source |       SS       df       MS              Number of obs =     278
-------------+------------------------------           F(  3,   274) =   43.38
       Model |   1.6757873     3  .558595768            Prob > F      =  0.0000
    Residual |  3.52855653   274  .012877944            R-squared     =  0.3220
-------------+------------------------------           Adj R-squared =  0.3146
       Total |  5.20434383   277  .018788245            Root MSE      =  .11348

------------------------------------------------------------------------------
         bmd |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0047303   .0015033    -3.15   0.002    -.0076897   -.0017709
      weight |   .0057653   .0005842     9.87   0.000     .0046152    .0069154
    cweight2 |  -.0000925   .0000239    -3.87   0.000    -.0001395   -.0000455
       _cons |    .724028   .1325897     5.46   0.000      .463004    .9850519
------------------------------------------------------------------------------
```

- Results for age unchanged, effect of weight more precisely estimated

Model selection algorithms

- Procedures for selecting predictors on statistical grounds, some implemented in Stata:
  - univariate screening; change-in-estimate criterion; backwards, forwards, and stepwise selection
- Epidemiologists and statisticians both uncomfortable with these methods
- For goal 1, screening with cross-validation works better
- For goals 2 and 3, DAG-based procedures preferable

Screening with single predictor models (AKA univariate screening)

- Screen using single-predictor models, retain predictors with *p*-value less than some criterion (e.g. $p<0.1$)
- Use a liberal retention criterion to avoid missing negatively confounded variables
- Initial list should reflect substantive considerations
- Can be useful for reducing the number of covariates (but better done a priori)

Change-in-estimate criterion

- Force in strongly motivated *A*-list predictors; delete *B*-list predictors if omission changes coefficient for primary predictor by < 5 or 10% (goal 2)
- Advantages:
  - reflects empirical criterion for confounding
  - can be integrated with DAG-based procedures – now implemented in Stata `cic` command (see lab 7)
- Disadvantage: defining A- and B-lists often challenging)

Backward stepwise selection

- Backward selection
  - Start from big model including all candidate predictors
  - Variables can be forced in
  - Sequentially delete predictor with biggest p-value and re-fit model
  - Stop when all remaining variables meet inclusion criterion (e.g., $p < 0.2$)

- Advantages: should do well with negative confounding
- Disadvantages:
  - initial model could be unstable if too large
  - selections subject to chance, especially between co-linear variables
  - sequential algorithm, so good models may be missed

Forward stepwise selection

- Start from minimum set of variables (i.e., the "*A*-list")
- Sequentially add omitted predictor with smallest *p*-value
- Stop when no more variables meet inclusion criterion
- Stepwise also allows variables to be deleted
- Advantages: Avoids problem with too-large initial model
- Disadvantages:
  - results may be affected by negative confounding

Categorical variables in stepwise selection procedures

- Selection procedures should keep indicator variables for all categories together - can use parentheses to force this in Stata:

```
xi: stepwise, pr(.2):  regress outcome x1 (i.x2) x3 x4
```

  - uses F test to decide to keep or drop all levels of x_2
  - note that `xi:` prefix is required
  - command `stepwise` can be abbreviated as `sw`
- *Note*: collapsing categories post hoc inflates type-I error

Pitfalls of automated model selection

- *P*-values too small, CIs too narrow, but hard to fix (type-I error rate inflated by searching over many models)
- Testimation bias: coefficient estimates biased away from null, especially for weak predictors
- Only complete cases used in automated procedures (i.e., no missings on any predictors in initial list)
- Poorly motivated, unstable choices between predictors

A priori model selection (preferred)

- Select MSAS based on well-motivated DAG
- *Advantages*
  - avoids pitfalls of model selection
  - *p*-values retain their theoretical meaning – defensible on substantive grounds
- *Disadvantages*
  - more suitable for well-studied areas; DAG, MSAS may be controversial
  - opens door to residual confounding if important variables, arrows are omitted from DAG
- Still requires checking selected model for unmodeled nonlinearities, omitted interactions

Conducting sensitivity analyses

- Multiple plausible DAGs: show whether substantive results differ by MSAS
- For statistically driven approaches, check sensitivity to
  - model selection procedure (forwards, backwards, stepwise)
  - model size / retention criterion
  - a priori variable choices (e.g., between collinear variables)

Summary Recommendations

- *Goal 1* – prediction: select model using aggressive search plus cross-validation/bootstrapping, validate in external sample
- *Goal 2* – predictor of primary interest: adjust for MSAS based on a strongly-motivated DAG; use change-in-estimate criterion or sensitivity analysis to deal with weakly motivated predictors
- *Goal 3* – identifying multiple independent predictors: treat each predictor as primary in turn, using methods for Goal 2; *or*, use an inclusive model, interpret weak findings cautiously
- Numbers of predictors: relax the 10-OBV/EPV rule of thumb if necessary to rule out confounding, but check for bad behavior
- Co-linearity:
  - between control variables, not a problem
  - between a predictor of primary interest and a non-ignorable confounder, may mean defeat
- Use sensitivity analyses