Extended sibships

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Classic Twin Design

- ACE / ADE
  - heterogeneity
  - multivariate
  - Sibling interaction
  - Developmental
- Issues
  - generalizibility >Additional Siblings
  - Assortative mating >Parents/spouses
  - Cultural transmission >Parents

Twins share the same womb at the same time, this may not only make them more similar, but sharing the womb itself may also lead to complications specific to twin births, rendering twins unrepresentative of the normal population

Due to assortative mating, DZ twin correlations will rise, leading to increased estimates of C.

Cultural transmission may lead to GE covariance in the offspring

Random vs Assortative Mating

- Random mating
  - Assortment will increase DZ correlations
  - When fitting ACE model, with assortment present, C will be overestimated
  - When fitting AE model, with assortment present, A will be overestimated

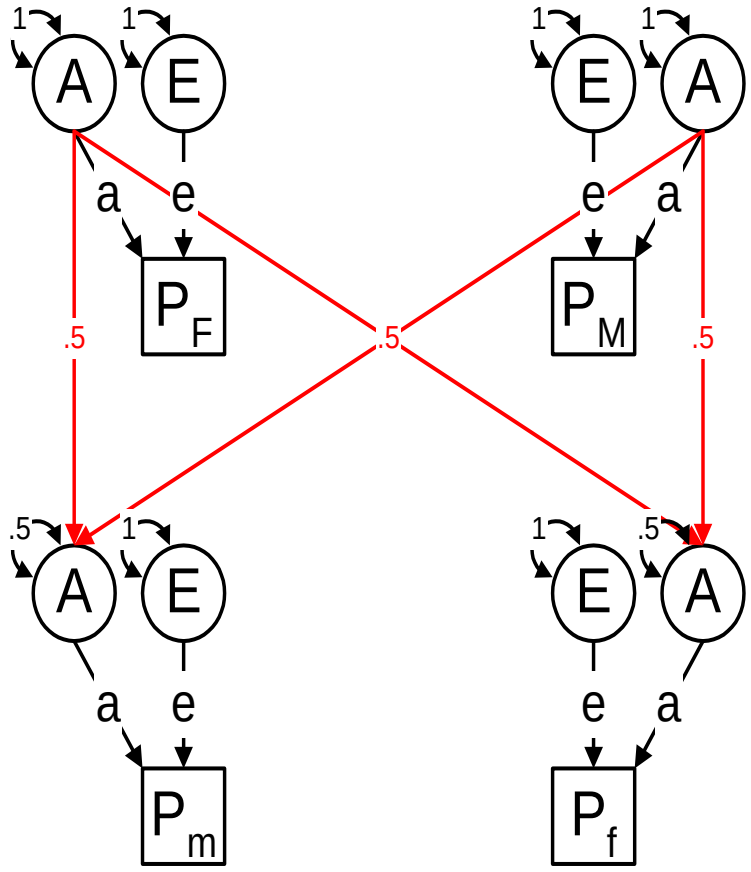
There is more than the classical twin design

- Larger pedigrees
  - Parent-offspring (incl. cultural transmission, assortative mating)
  - Grandparents-parents-offspring
  - Spouses of co-twins/siblings
  - Larger sibships
- Adoption studies
  - MZA DZA MZT DZT
  - Non-biological siblings
  - Virtual twins (non-biological siblings of same age)

Parent - Offspring

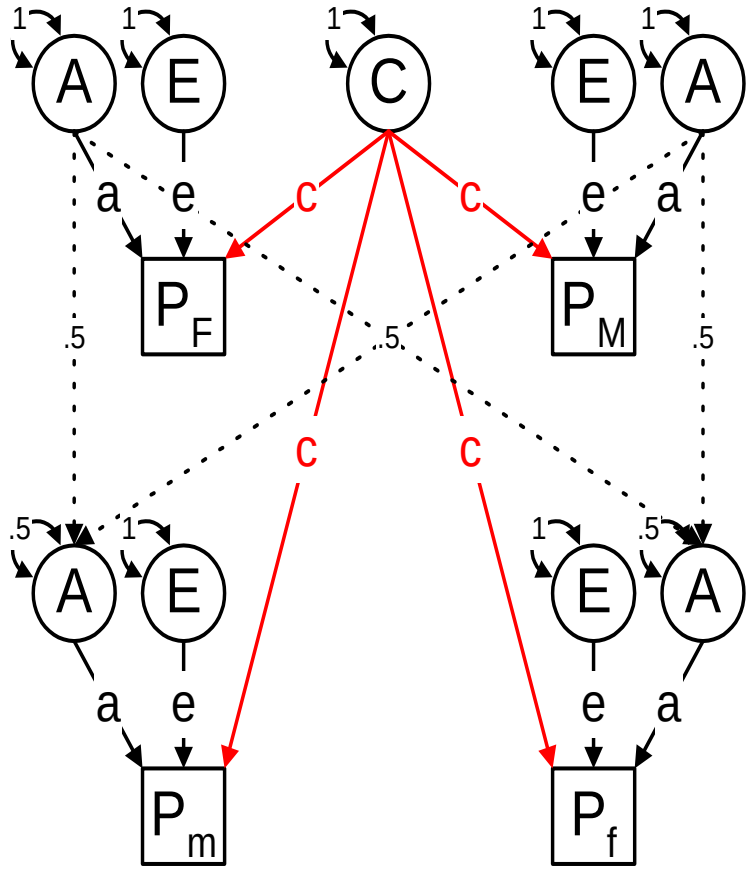
Genetic Transmission Model

- Genetic transmission
  - Fixed at .5
- Residual Genetic Variance
  - Fixed at .5
  - Equilibrium of variances across generations



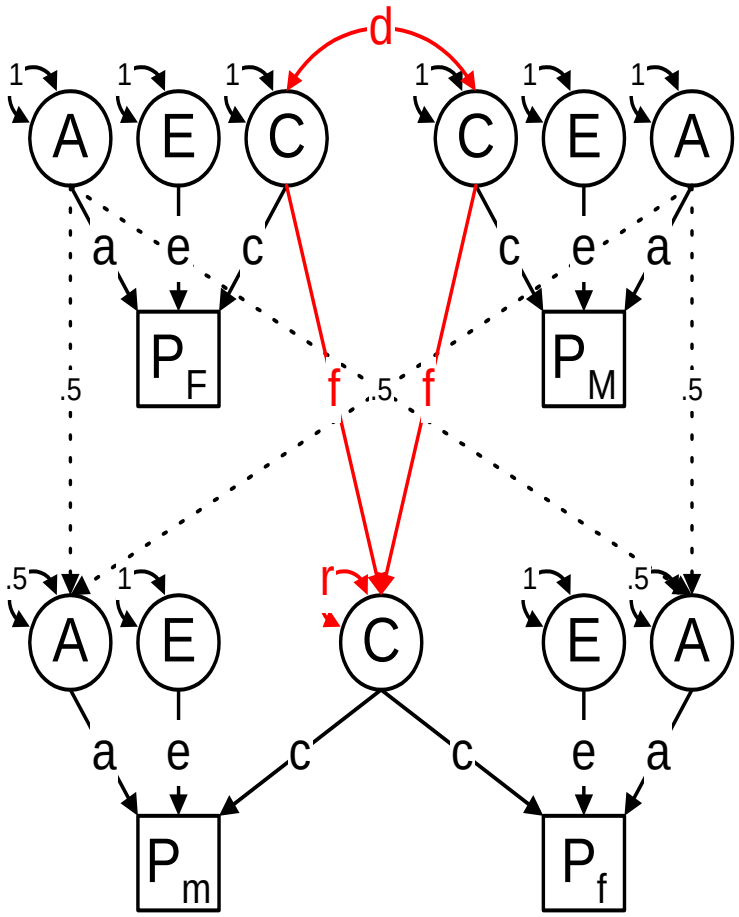
Common Environment Model

- Common environment
  - Same for all family members
- Assortment
  - Function of common environment



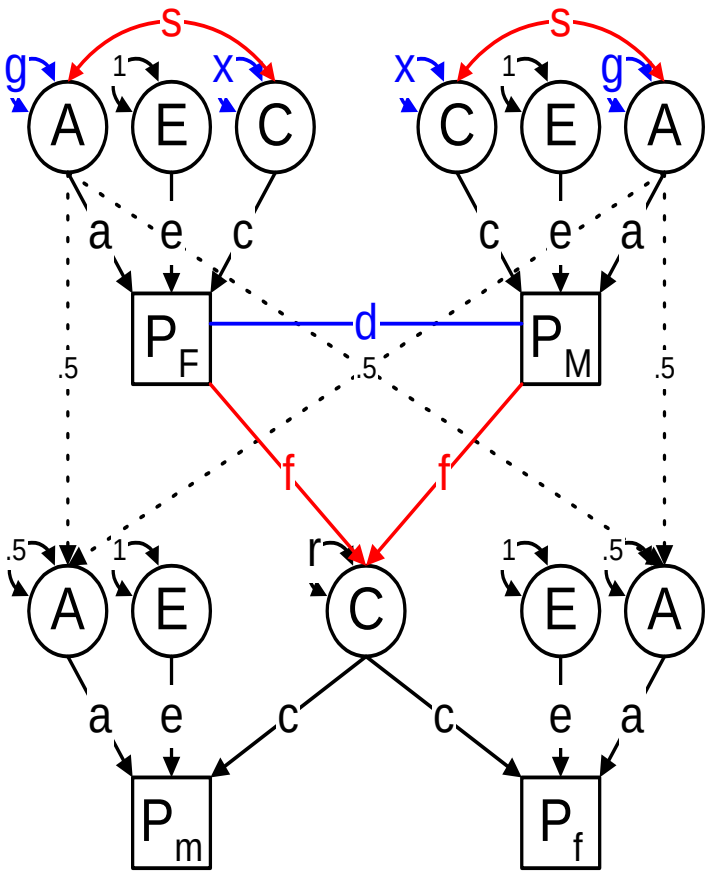
Social Homogamy Model

- Assortment
  - Social
- Cultural Transmission
  - From C to C
- Non-parental Shared Environment
  - Residual



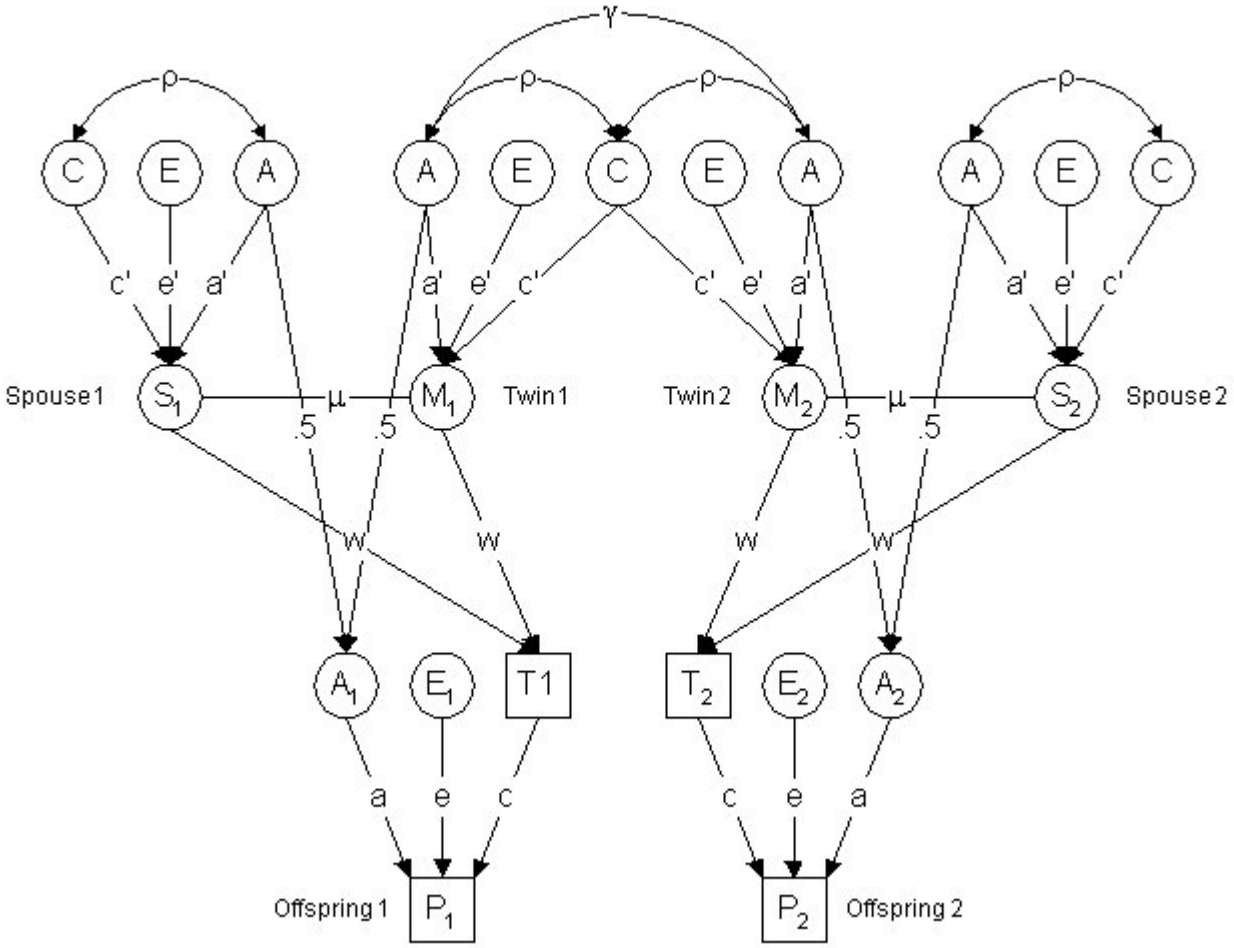
Phenotypic Assortment Model

- Assortment
  - Phenotypic
- Cultural Transmission
  - From P to C
- Non-parental Shared Environment
  - Residual
- Genotype-Environment Covariance



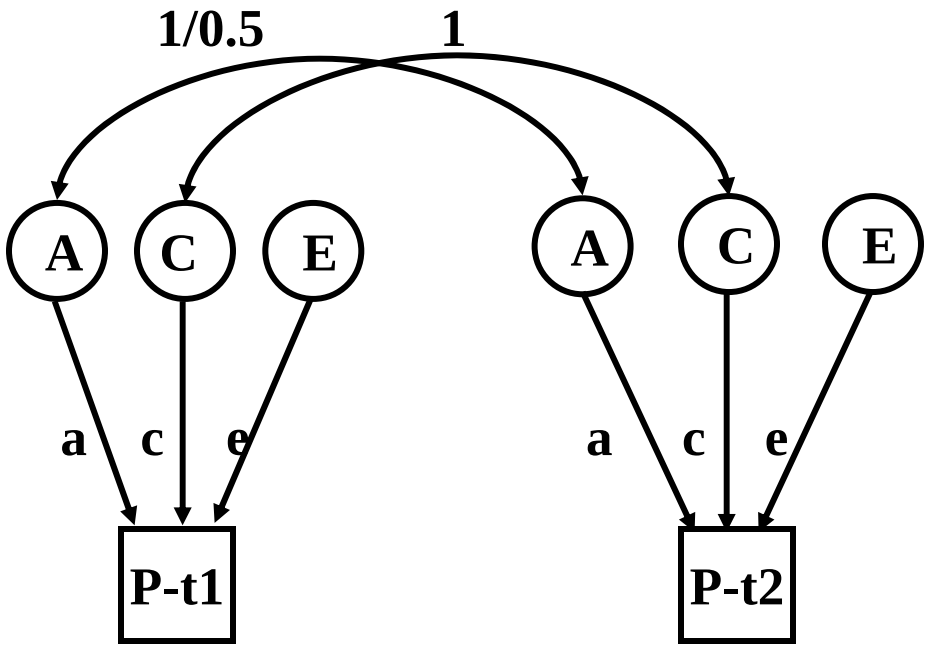
Spouses and offspring of twins

Model for spouses and children of twins (Eaves)



Extended sibships

Twins Only



Twins Only: var-cov matrices

MZ

	t1	t2
t1	$a^2+c^2+e^2$	a^2+c^2
t2	a^2+c^2	$a^2+c^2+e^2$

In Mx:

MZ group:

```
A+C+E  | A+C_
A+C    | A+C+E ;
```

DZ

	t1	t2
t1	$a^2+c^2+e^2$	$0.5a^2+c^2$
t2	$0.5a^2+c^2$	$a^2+c^2+e^2$

In Mx:

DZ group:

```
A+C+E  | H@A+C_
H@A+C| A+C+E ;
```

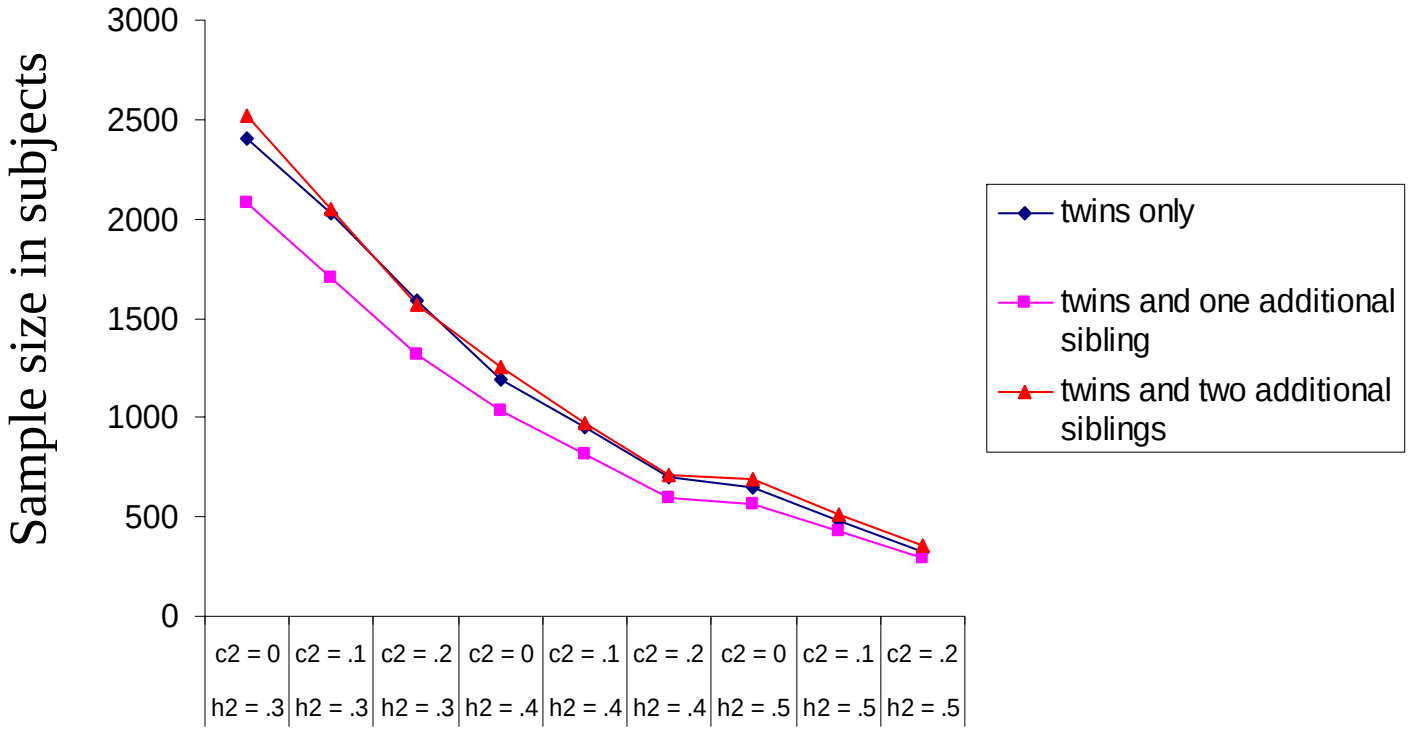
Adding siblings

Is easy!

But why should I?

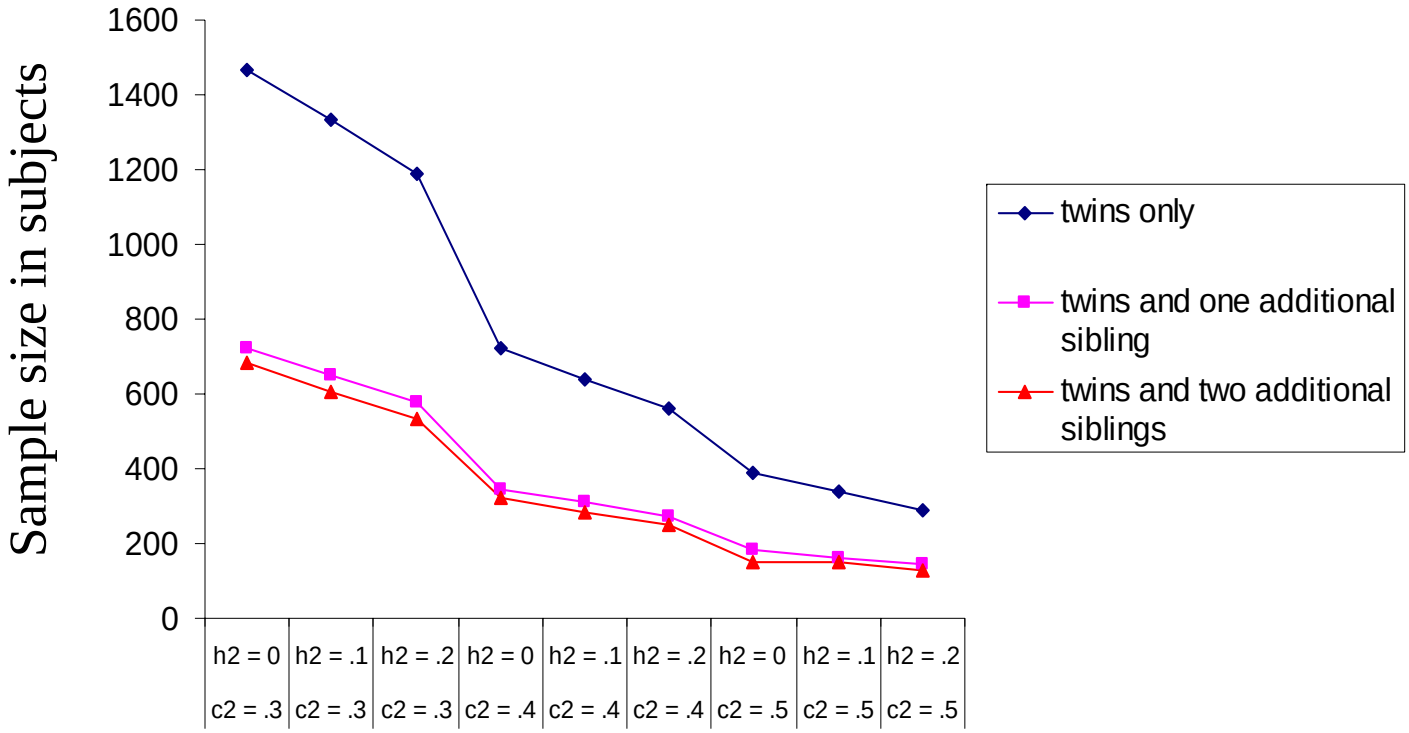
Sample size required to detect A

With power of 80% and probability of 5%



Sample size required to detect C

With power of 80% and probability of 5%



Larger sibships

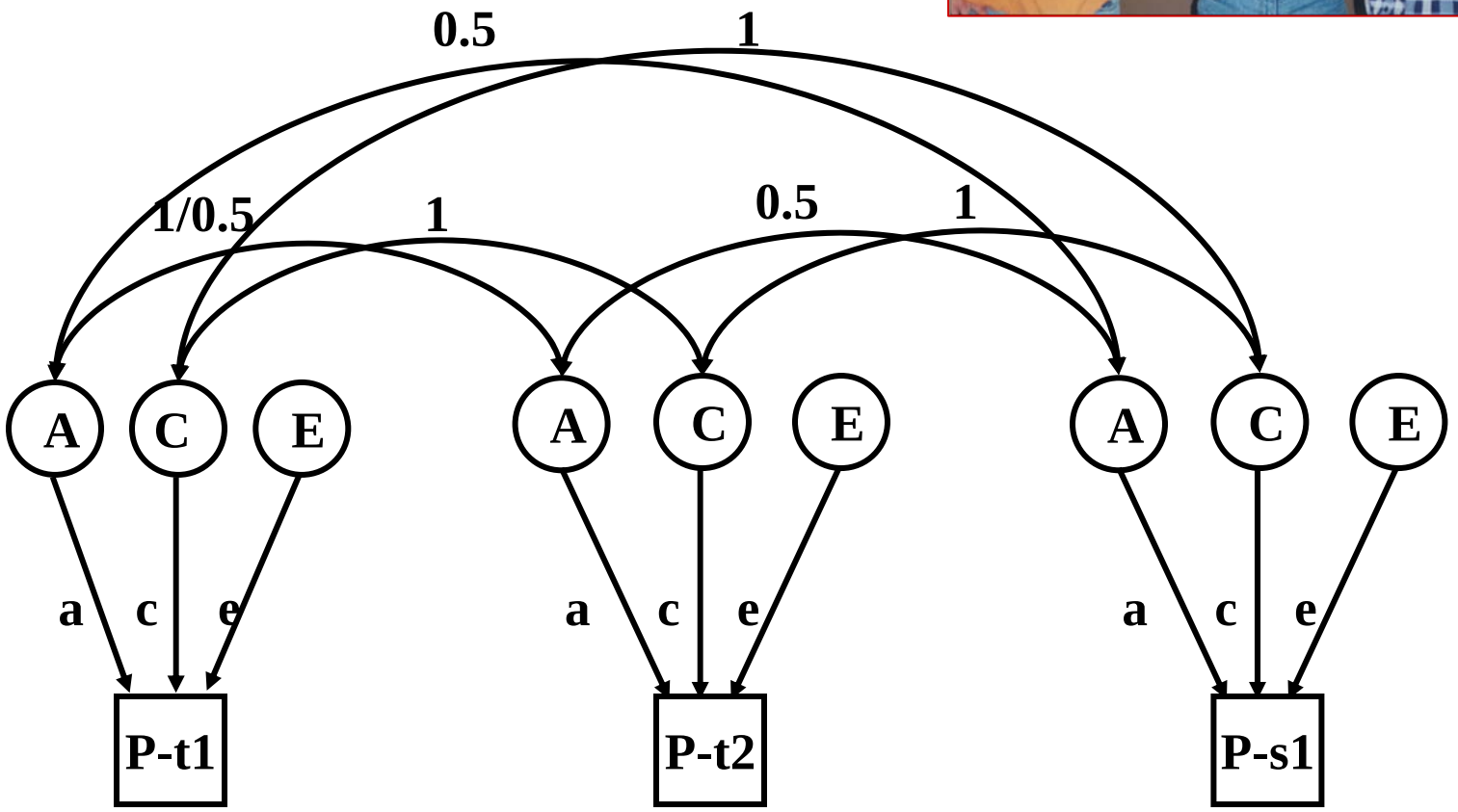
- Provides a bit more power to detect A
- Provides a lot more power to detect C

Since C is usually small (e.g. A = .60, C = .20, E = .20), C is usually dropped from the model as it is not significant. As C is a familial source of variance, part of it will the end up in A, which will now be overestimated. Therefore, more power for C protects against overestimation of A.

Larger sibships

- Will also allow you to test certain assumptions such as:
  - Are twins different from singletons with respect to means?
  - Are twins different from singletons with respect to variances?
  - Do DZ twins correlate any different than non-twin sibpairs?

Adding siblings



MZ and one additional sibling

	t1	t2	s1
t1	$a^2+c^2+e^2$	a^2+c^2	$0.5a^2+c^2$
t2	a^2+c^2	$a^2+c^2+e^2$	$0.5a^2+c^2$
s1	$0.5a^2+c^2$	$0.5a^2+c^2$	$a^2+c^2+e^2$

DZ and one additional sibling

	t1	t2	s1
t1	$a^2+c^2+e^2$	$0.5a^2+c^2$	$0.5a^2+c^2$
t2	$0.5a^2+c^2$	$a^2+c^2+e^2$	$0.5a^2+c^2$
s1	$0.5a^2+c^2$	$0.5a^2+c^2$	$a^2+c^2+e^2$

Exercise

- Copy TwinsOnly.mx and mriiq.rec
- Open Mx script TwinsOnly.mx

Modify this script such that

- Data from sib 1 is included
- Data from sib 1 to sib 6 are included
- Check –2ll, df, estimated pms, n observations for each model

	-2ll	df	est	obs
Twins	3878.177	494	4	498
Twins +1	5025.192	639	4	643
Twins +6	5388.980	684	4	688

Adding more siblings becomes tedious!

(and errorprone..)

MZ's and 6 additional siblings

A+C+E | A+C | H@A+C |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

A+C | A+C+E | H@A+C |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

H@A+C | H@A+C | A+C+E |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

H@A+C | H@A+C | H@A+C | A+C+E | H@A+C |H@A+C | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | A+C+E |H@A+C | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |A+C+E | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |H@A+C | A+C+E | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |H@A+C | H@A+C | A+C+E ;

Adding more siblings

6 extra siblings

MZ's and 6 additional siblings

A+C+E | A+C | H@A+C |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

A+C | A+C+E | H@A+C |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

H@A+C | H@A+C | A+C+E |H@A+C | H@A+C |H@A+C | H@A+C |H@A+C _

H@A+C | H@A+C | H@A+C | A+C+E | H@A+C |H@A+C | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | A+C+E |H@A+C | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |A+C+E | H@A+C | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |H@A+C | A+C+E | H@A+C __

H@A+C | H@A+C | H@A+C | H@A+C | H@A+C |H@A+C | H@A+C | A+C+E ;

MZ's and 6 additional siblings

$$
\begin{bmatrix}
1 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
1 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 1 & 0.5 & 0.5 \\
0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 1 & 0.5 \\
0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 & 1
\end{bmatrix}
@ A =
\begin{bmatrix}
A & A & 0.5A & 0.5A & 0.5\,A & 0.5A & 0.5A & 0.5A \\
A & A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A
\end{bmatrix}
$$

$$Q@A$$

Twin pair and 6 additional siblings

1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1_
1|1|1|1|1|1|1|1;

@ C =

C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C_
C|C|C|C|C|C|C|C;

S@C, S Unit 8 8

Twin pair and 6 additional siblings

1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 _		E | 0 | 0 | 0 | 0 | 0 | 0 | 0 _
0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 _		0 | E | 0 | 0 | 0 | 0 | 0 | 0 _
0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 _		0 | 0 | E | 0 | 0 | 0 | 0 | 0 _
0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 _	@ E =	0 | 0 | 0 | E | 0 | 0 | 0 | 0 _
0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 _		0 | 0 | 0 | 0 | E | 0 | 0 | 0 _
0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 _		0 | 0 | 0 | 0 | 0 | E | 0 | 0 _
0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 _		0 | 0 | 0 | 0 | 0 | 0 | E | 0 _
0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 ;		0 | 0 | 0 | 0 | 0 | 0 | 0 | E ;

T@E, T = Ident 8 8

Mx

- Copy Twins&6.mx
- Open Twins&6.mx

Exercise

- Modify this script for maximum nr of siblings = 3, 4, or 5, write down –2ll, df, estimated pms, n observations for each model

	-2ll	df	est	obs
Twins	3878.177	494	4	498
Twins +1	5025.192	639	4	643
Twins +2	5279.002	671	4	675
Twins +3	5337.380	678	4	682
Twins +4	5374.617	682	4	686
Twins +5	5381.883	683	4	687
Twins +6	5388.980	684	4	688

Exercise

- Modify the script with 6 additional siblings (so 8 persons) to a bivariate script for wmem and greym. If correct:
- -2ll=8083.085, df = 935
- You can start the mean for wmem at 60 and the mean for greym at 400. all variance components (SD) can be started at 30
- Add standardization matrices for A and E

In Summary

- Be aware of assumptions of the twin design
- Adding additional persons: add expectations to Covariance statement
- Adding additional phenotypes: change matrix dimensions