# Extended sibships

Danielle Posthuma
Kate Morley
Files: \\danielle\Sibs

# 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 A; cultural transmission may lead to CE covariance in the offspring

# 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 models

Genetic transmission model
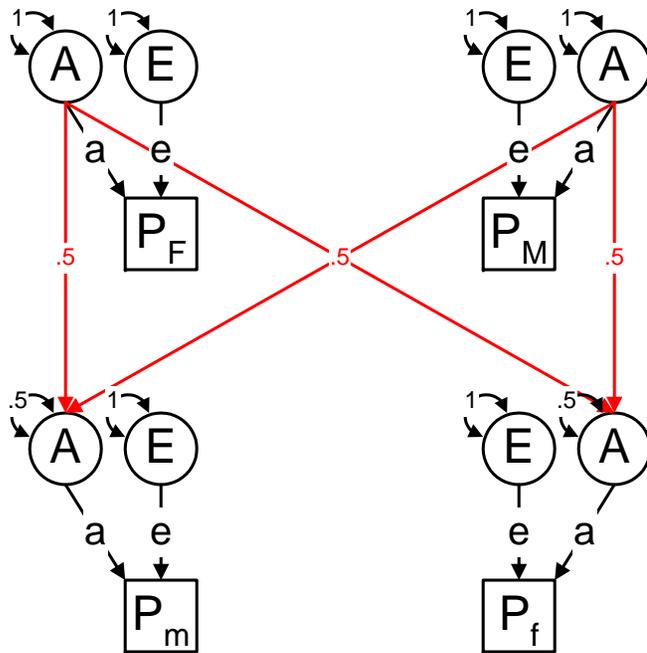
Social homogamy model
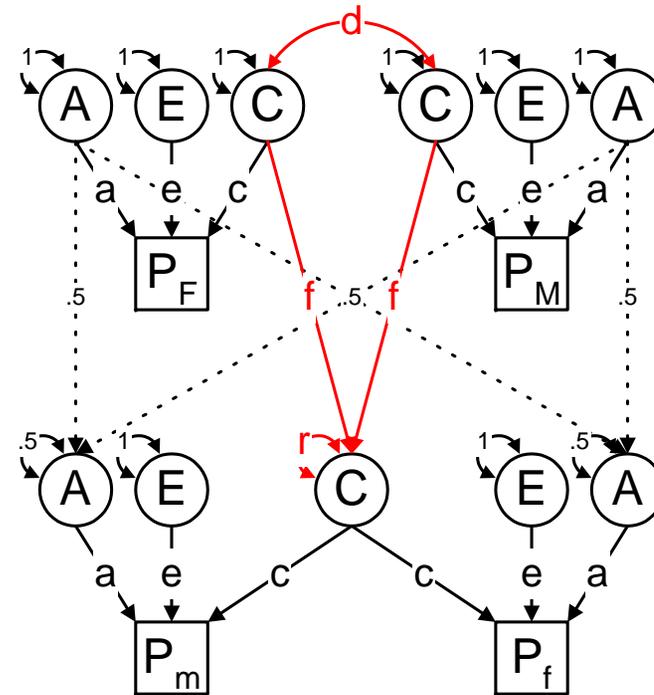
# Model for spouses and children of twins (Eaves)
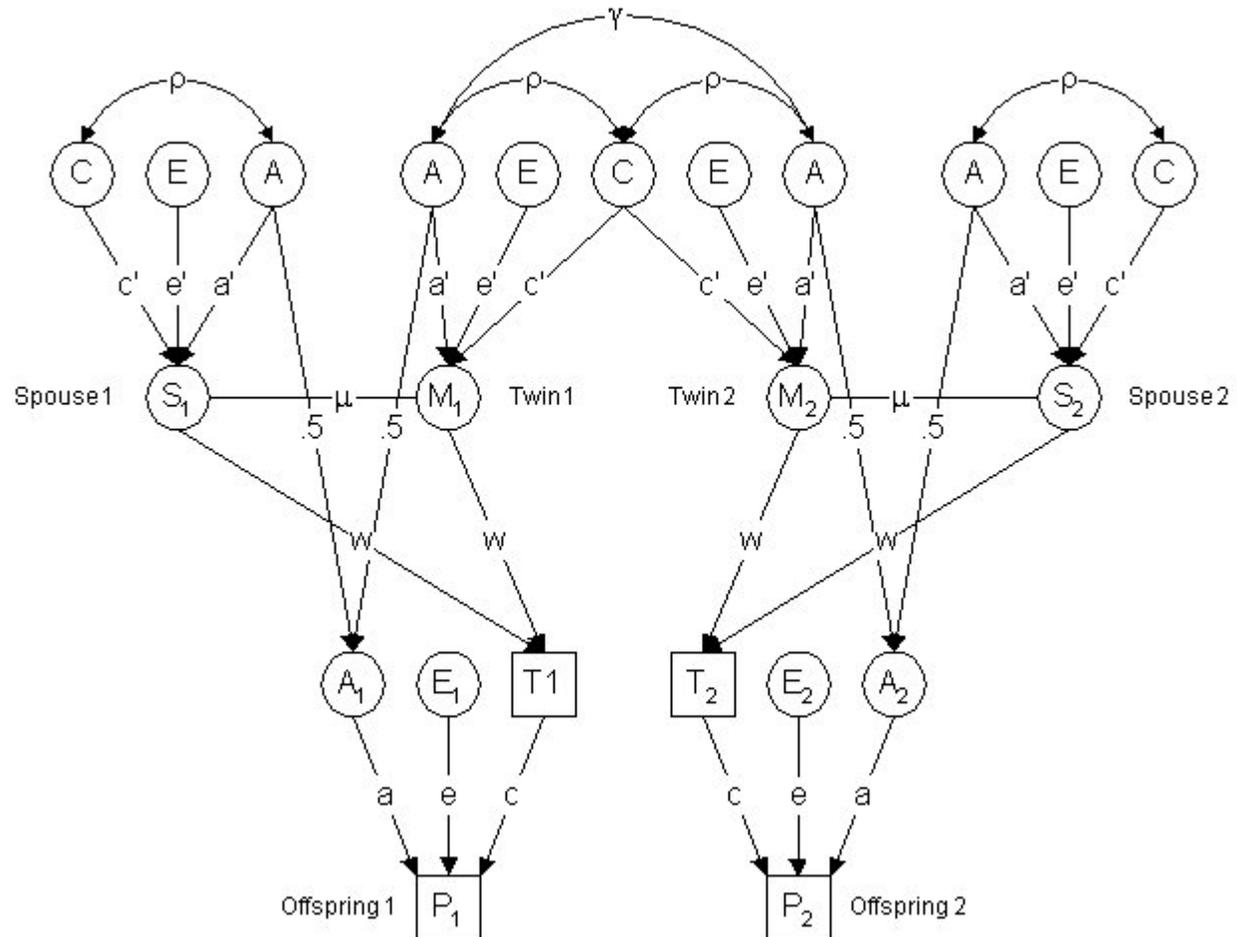
# Extended sibships

# Twins Only



**1/0.5**   **1**

```
   A   C   E        A   C   E
    \  |  /          \  |  /
   a   c   e        a   c   e
    \  |  /          \  |  /
   ┌──────┐        ┌──────┐
   │ P-t1 │        │ P-t2 │
   └──────┘        └──────┘
```
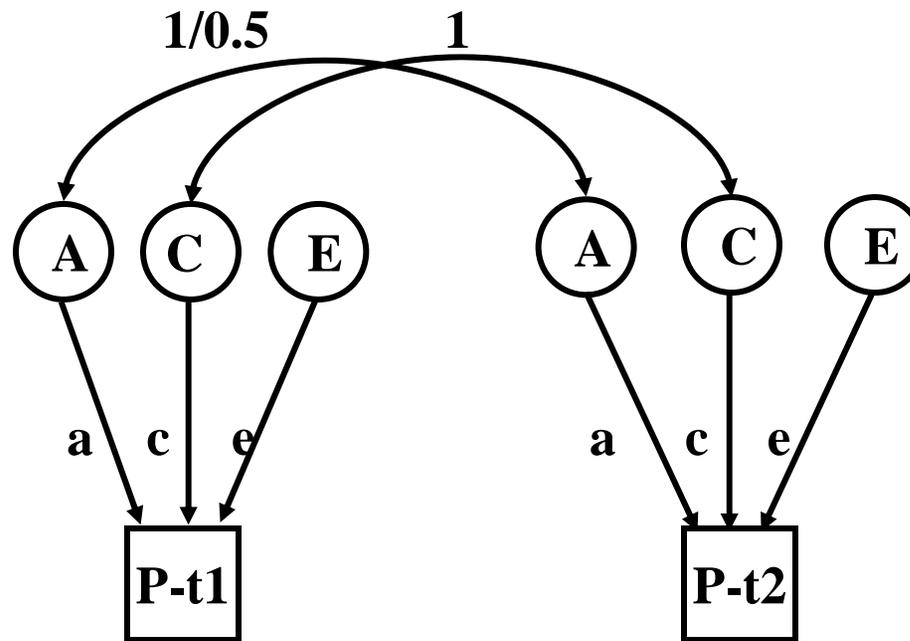
# Twins Only: var-cov matrices

**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%
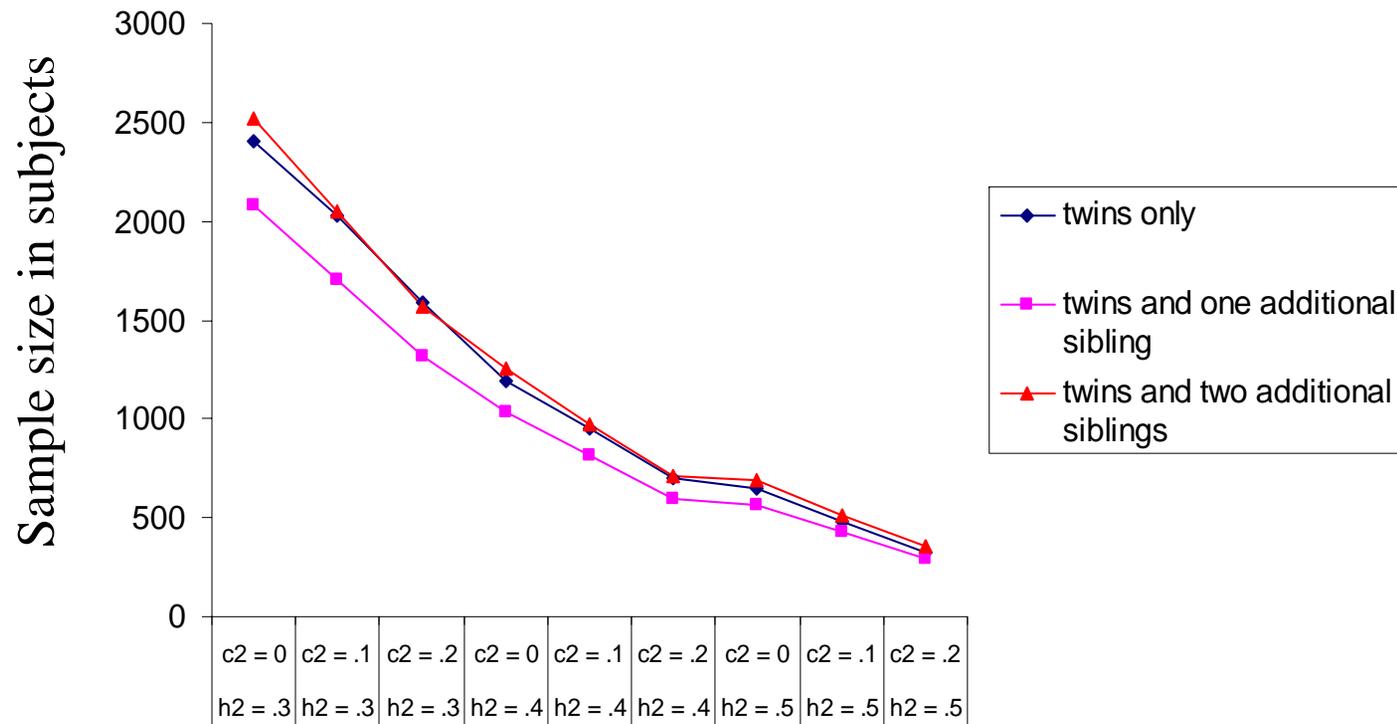
# Sample size required to detect C
## With power of 80% and probability of 5%
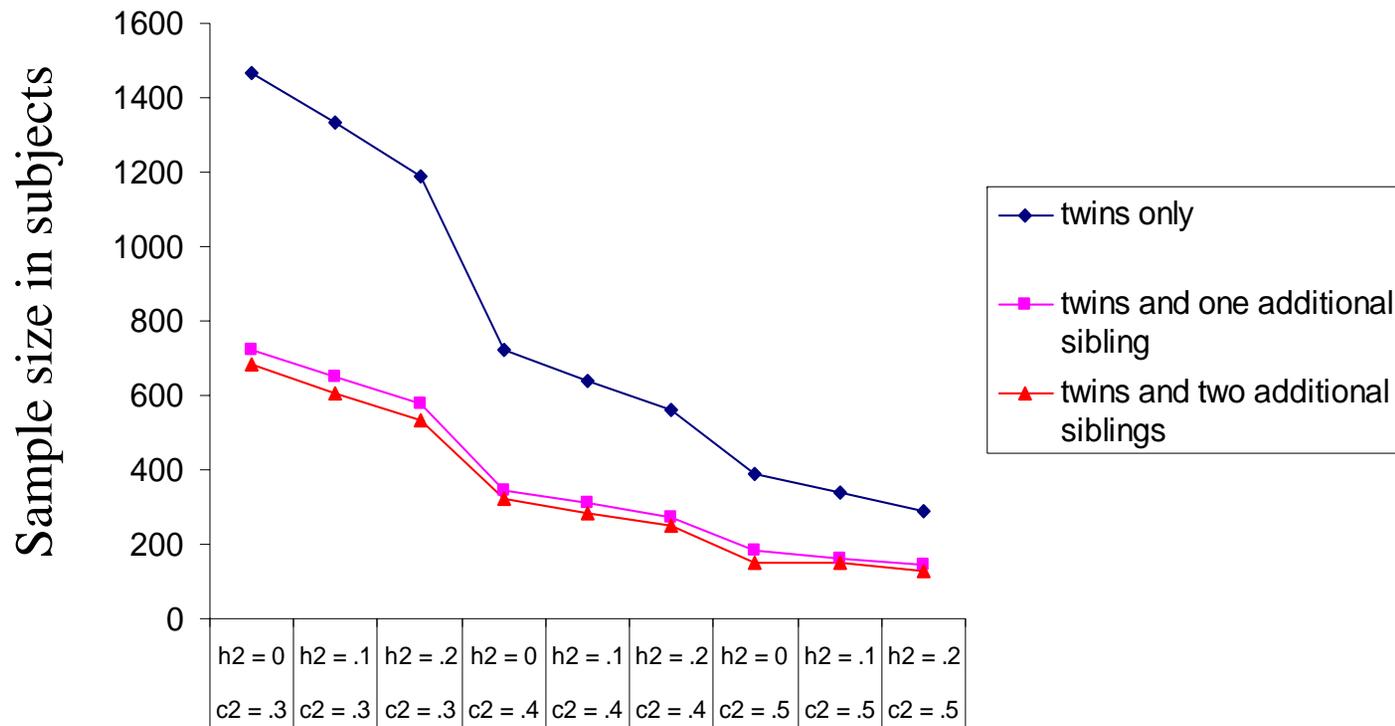
# Larger sibships

- 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



0.5    1

1/0.5    1    0.5    1

(A) (C) (E)    (A) (C) (E)    (A) (C) (E)

a  c  e    a  c  e    a  c  e

P-t1    P-t2    P-s1
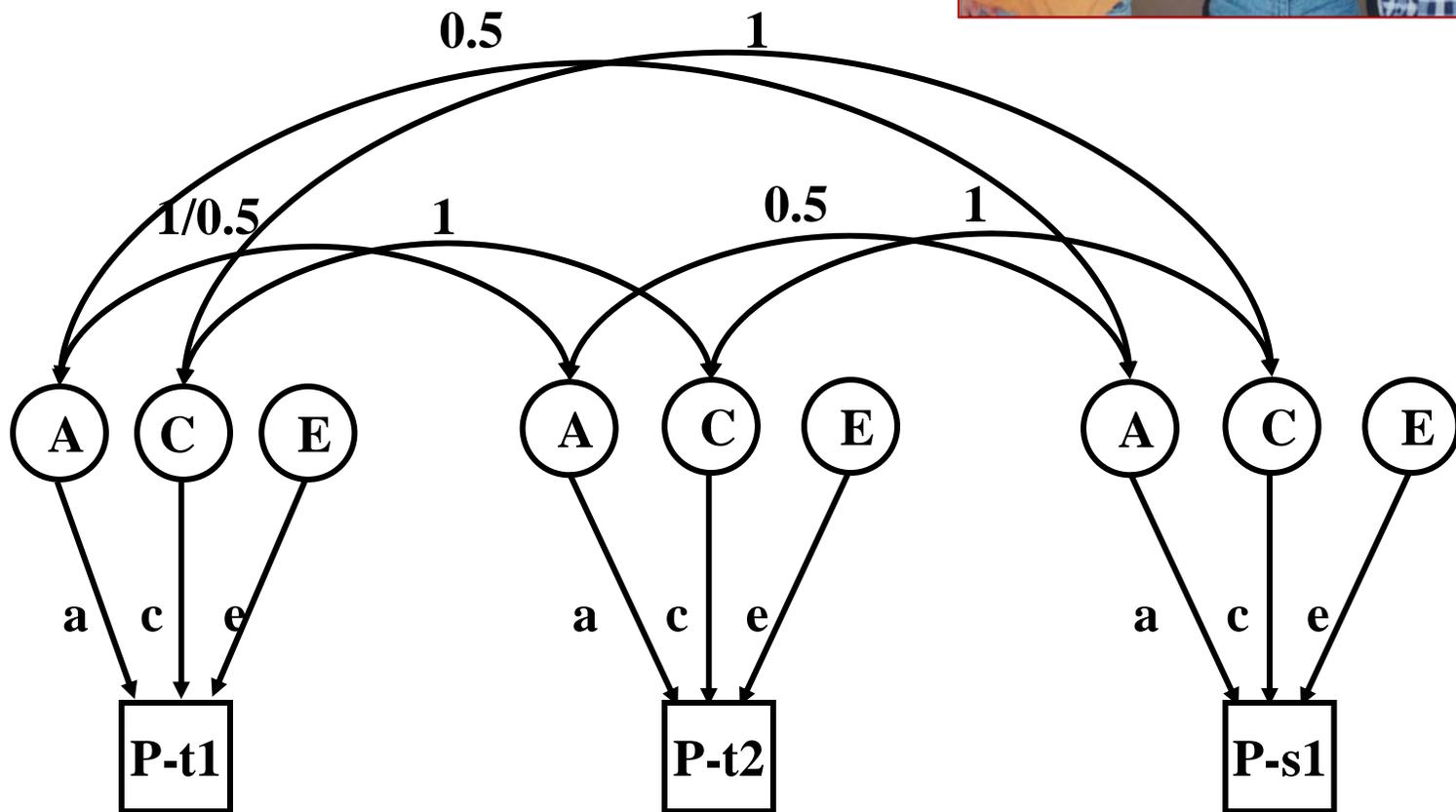
## MZ and one additional sibling

|     | 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

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 _     @ $A =$
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 ;

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 ;

$Q @ A$

# Twin pair and 6 additional siblings

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _   @ C =   C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 _           C|C|C|C|C|C|C|C _

1|1|1|1|1|1|1|1 ;           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

- Adding additional persons: add expectations to Covariance statement

- Adding additional phenotypes: change matrix dimensions