Extended sibships

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Files: \danielle\ExtSibs
**Classic Twin Design**

- **ACE / ADE**
  - heterogeneity
  - multivariate
  - Sibling interaction
  - Developmental

- **Issues**
  - generalizability > Additional Siblings
  - Assortative mating > Parents/spouses
  - Cultural transmission > Parents

Due to assortative mating, DZ twin correlations will rise, leading to increased estimates and misspecification may lead to GE covariance in the offspring.

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.
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

<table>
<thead>
<tr>
<th></th>
<th>MZ</th>
<th>DZ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t1</td>
<td>t2</td>
</tr>
<tr>
<td></td>
<td>a(^2)c(^2) + e(^2)</td>
<td>a(^2)c(^2)</td>
</tr>
<tr>
<td>t1</td>
<td>a(^2)c(^2)</td>
<td>a(^2)c(^2)</td>
</tr>
<tr>
<td>t2</td>
<td>a(^2)c(^2)</td>
<td>a(^2)c(^2)+e(^2)</td>
</tr>
</tbody>
</table>

**In Mx:**

**MZ group:**

\[
\begin{align*}
A+C+E & | A+C_ \\
A+C & | A+C+E \\
\end{align*}
\]

**DZ group:**

\[
\begin{align*}
A+C+E & | H@A+C_ \\
H@A+C & | A+C+E \\
\end{align*}
\]
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 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

<table>
<thead>
<tr>
<th></th>
<th>t1</th>
<th>t2</th>
<th>s1</th>
</tr>
</thead>
<tbody>
<tr>
<td>t1</td>
<td>$a^2+c^2+e^2$</td>
<td>$a^2+c^2$</td>
<td>$0.5a^2+c^2$</td>
</tr>
<tr>
<td>t2</td>
<td>$a^2+c^2$</td>
<td>$a^2+c^2+e^2$</td>
<td>$0.5a^2+c^2$</td>
</tr>
<tr>
<td>s1</td>
<td>$0.5a^2+c^2$</td>
<td>$0.5a^2+c^2$</td>
<td>$a^2+c^2+e^2$</td>
</tr>
</tbody>
</table>

### DZ and one additional sibling

<table>
<thead>
<tr>
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<th>t1</th>
<th>t2</th>
<th>s1</th>
</tr>
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<tbody>
<tr>
<td>t1</td>
<td>$a^2+c^2+e^2$</td>
<td>$0.5a^2+c^2$</td>
<td>$0.5a^2+c^2$</td>
</tr>
<tr>
<td>t2</td>
<td>$0.5a^2+c^2$</td>
<td>$a^2+c^2+e^2$</td>
<td>$0.5a^2+c^2$</td>
</tr>
<tr>
<td>s1</td>
<td>$0.5a^2+c^2$</td>
<td>$0.5a^2+c^2$</td>
<td>$a^2+c^2+e^2$</td>
</tr>
</tbody>
</table>
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 $-2\text{ll}$, df, estimated pms, n observations for each model
<table>
<thead>
<tr>
<th></th>
<th>-2ll</th>
<th>df</th>
<th>est</th>
<th>obs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twins</td>
<td>3878.177</td>
<td>494</td>
<td>4</td>
<td>498</td>
</tr>
<tr>
<td>Twins +1</td>
<td>5025.192</td>
<td>639</td>
<td>4</td>
<td>643</td>
</tr>
<tr>
<td>Twins +6</td>
<td>5388.980</td>
<td>684</td>
<td>4</td>
<td>688</td>
</tr>
</tbody>
</table>
Adding more siblings becomes tedious!
(and errorprone..)

**MZ’s and 6 additional siblings**

<table>
<thead>
<tr>
<th>A+C+E</th>
<th>A+C</th>
<th>H@A+C</th>
<th>H@A+C</th>
<th>H@A+C</th>
<th>H@A+C</th>
<th>H@A+C</th>
</tr>
</thead>
<tbody>
<tr>
<td>A+C</td>
<td>A+C+E</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
</tr>
<tr>
<td>H@A+C</td>
<td>H@A+C</td>
<td>A+C+E</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
</tr>
<tr>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>A+C+E</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
</tr>
<tr>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>A+C+E</td>
<td>H@A+C</td>
<td>H@A+C</td>
</tr>
<tr>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>H@A+C</td>
<td>A+C+E</td>
<td>H@A+C</td>
<td>A+C+E</td>
</tr>
</tbody>
</table>
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 | 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 | 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 |
MZ’s and 6 additional siblings

\[
\begin{array}{cccccccc}
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
0.5 & 0.5 & 1 & 0.5 & 0.5 & 0.5 & 0.5 & 0.5 \\
\end{array}
\]

\[
\begin{array}{cccccccc}
A & A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A \\
A & A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A & 0.5A \\
0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & 0.5A & A \\
\end{array}
\]

\[
\begin{array}{cccccccc}
\text{Q@A}
\end{array}
\]
Twin pair and 6 additional siblings

\[
\begin{align*}
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1_ & \quad C|C|C|C|C|C|C|C_ \\
1|1|1|1|1|1|1|1; & \quad C|C|C|C|C|C|C|C;
\end{align*}
\]

\[S@C, S \text{ Unit 8 8}\]
Twin pair and 6 additional siblings

\[
\begin{array}{cccccccc}
1 & 0 & 0 & 0 & 0 & 0 & 0 & _ \\
0 & 1 & 0 & 0 & 0 & 0 & 0 & _ \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & _ \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & _ \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & _ \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & _ \\
0 & 0 & 0 & 0 & 0 & 0 & 1 ; \\
\end{array}
\]

\[
\begin{array}{cccccccc}
E & 0 & 0 & 0 & 0 & 0 & 0 & _ \\
0 & E & 0 & 0 & 0 & 0 & 0 & _ \\
0 & 0 & E & 0 & 0 & 0 & 0 & _ \\
0 & 0 & 0 & E & 0 & 0 & 0 & _ \\
0 & 0 & 0 & 0 & E & 0 & 0 & _ \\
0 & 0 & 0 & 0 & 0 & E & 0 & _ \\
0 & 0 & 0 & 0 & 0 & 0 & E ; \\
\end{array}
\]

\[T@E, \; T = \text{Ident} \; 8 \; 8\]
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
<table>
<thead>
<tr>
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<td>Twins +1</td>
<td>5025.192</td>
<td>639</td>
<td>4</td>
<td>643</td>
</tr>
<tr>
<td>Twins +2</td>
<td>5279.002</td>
<td>671</td>
<td>4</td>
<td>675</td>
</tr>
<tr>
<td>Twins +3</td>
<td>5337.380</td>
<td>678</td>
<td>4</td>
<td>682</td>
</tr>
<tr>
<td>Twins +4</td>
<td>5374.617</td>
<td>682</td>
<td>4</td>
<td>686</td>
</tr>
<tr>
<td>Twins +5</td>
<td>5381.883</td>
<td>683</td>
<td>4</td>
<td>687</td>
</tr>
<tr>
<td>Twins +6</td>
<td>5388.980</td>
<td>684</td>
<td>4</td>
<td>688</td>
</tr>
</tbody>
</table>
Exercise

- Modify the script with 6 additional siblings (so 8 persons) to a bivariate script for wmem and greym. If correct:
  - $-2\text{ll}=8083.085$, 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