Heterogeneity

Hermine Maes

TC19

March 2006

Files to Copy to your Computer

- Faculty/hmaes/tc19/maes/heterogeneity
  - ozbmi.rec
  - ozbmi.dat
  - ozbmiysat(4)(5).mx
  - ozbmiyace(4)(eq)(5).mx
  - Heterogeneity.ppt

Goodness-of-Fit Statistics for BMI in young females

	-2LL	df	χ^2	df	p	AIC	χ^2	df	p
Sat	4055.93	1767							
ADE	4059.21	1770	3.28	3	.35	-2.72			
AE	4063.61	1771	7.68	4	.10	-0.32	4.40	1	.04
ACE	4063.61	1770	7.68	3	.05	1.68			
CE	4216.29	1771	160.	4	.00	152	152	1	.00
E	4585.59	1772	529.	5	.00	519	521	2	.00

Parameter Estimates for BMI in young females

	Path coefficients				Variance comp				Stand var comp			
	a	c	e	d	a^2	c^2	e^2	d^2	a^2	c^2	e^2	d^2
Sat												
ADE	.56		.41	.54	.31		.17	.29	.40		.22	.38
AE	.78		.42		.61		.17		.78		.22	
ACE	.78	.00	.42		.61	.00	.17		.78	.00	.22	
CE		.67	.56			.47	.32			.59	.41	
E			.88				.77				1.0	

Goodness-of-Fit Statistics for BMI in young males

	-2LL	df	χ^2	df	p	AIC	)	df	p
Sat	1939.72	900					χ^2		
ADE	1947.06	903	7.33	3	.06	1.33			
AE	1950.85	904	11.13	4	.02	3.12	3.80	1	.05
ACE	1950.85	903	11.13	3	.01	5.13			
CE	2036.99	904	97	4	.00	89	86	1	.00
E	2191.72	905	251	5	.00	241	240	2	.00

Parameter Estimates for BMI in young males

	Path coefficients				Variance comp				Stand var comp			
	a	c	e	d	a^2	c^2	e^2	d^2	a^2	c^2	e^2	d^2
Sat												
ADE	.49		.37	.54	.23		.14	.29	.35		.21	.43
AE	.73		.38		.54		.14		.79		.21	
ACE	.73	.00	.38		.54	.00	.14		.79	.00	.21	
CE		.59	.54			.35	.30			.54	.46	
E			.81				.65				1.0	

Heterogeneity Questions I

- Univariate Analysis: What are the contributions of additive genetic, dominance/shared environmental and unique environmental factors to the variance?
- Heterogeneity Analysis: Are the contributions of genetic and environmental factors equal for different groups, such as sex, race, ethnicity, SES, environmental exposure, etc.?

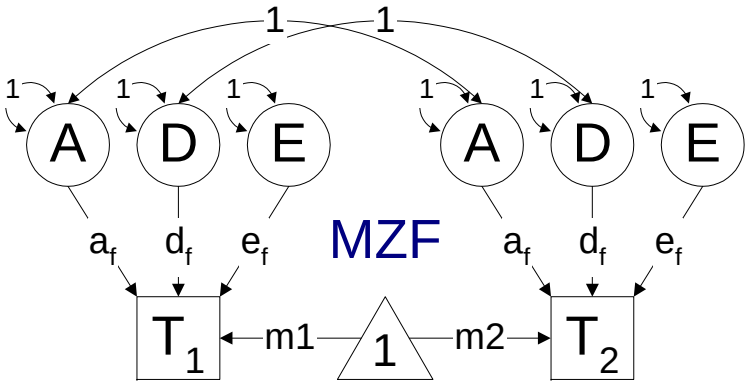
Heterogeneity Questions II

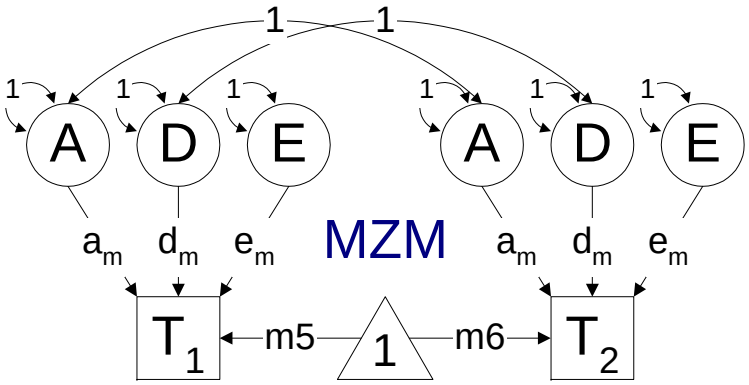
- Are these differences due to differences in the magnitude of the effects (quantitative)?
  - e.g. Is the contribution of genetic/environmental factors greater/smaller in males than in females?
- Are the differences due to differences in the nature of the effects (qualitative)?
  - e.g. Are there different genetic/environmental factors influencing the trait in males and females?

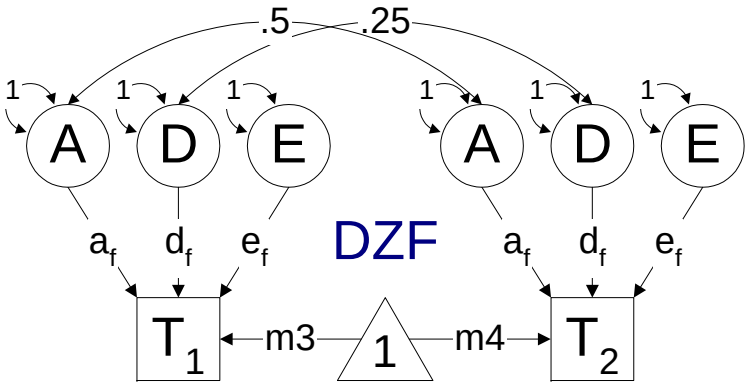
Groups

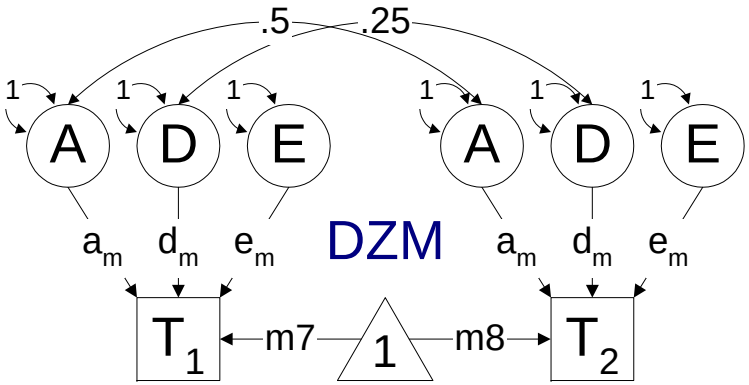
Comparison	Concordant for group membership	Discordant for group membership
gender	MZ & DZ: MM & FF pairs	DZ: opposite sex pairs
age	MZ & DZ: young & old pairs	
nationality	MZ & DZ: OZ & US pairs	
environment	MZ & DZ: urban & rural pairs	MZ & DZ: urban/ rural pairs

Heterogeneity









Females

Males

Heterogeneity Script

- #NGroups 8
- G1: female parameters
  - a_f, e_f, d_f
- G2: MZF data
  - m1, m2
- G3: DZF data
  - m3, m4
- G4: female standardized estimates
- G5: male parameters
  - a_m, e_m, d_m
- G6: MZM data
  - m5, m6
- G7: DZM data
  - m7, m8
- G8: male standardized estimates

Move Start Statements to Last Group

Models for Concordant Pairs

	G1 MZ	G1 DZ	G2 MZ	G2 DZ	EP
Saturated	v1 v2 cov m1 m2	v3 v4 cov m3 m4	v5 v6 cov m5 m6	v7 v8 cov m7 m8	12 + 8
Heterogeneity	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_2 d_2 e_2 m5 m6	a_2 d_2 e_2 m7 m8	6 + 8
Homogeneity					

EP: estimated parameters

df=6

Exercise I

- Run Saturated Model
  - ozbmiysat4.mx
- Run Heterogeneity Model
  - ozbmiyade4.mx

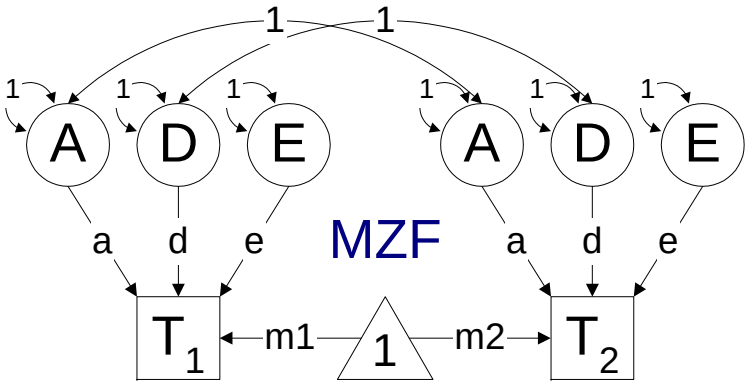
Goodness-of-Fit Statistics for BMI in young females+males

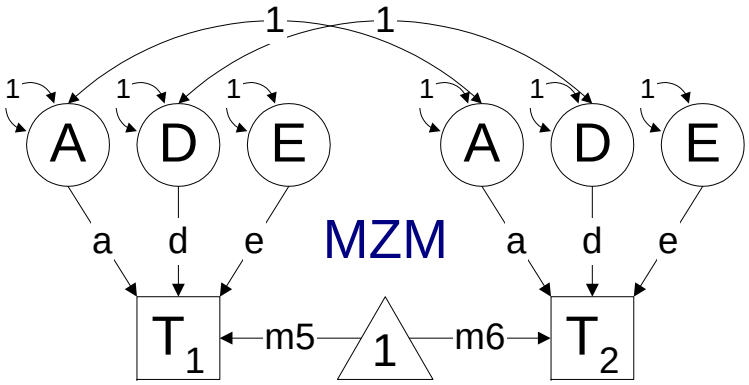
	-2LL	df	χ^2	df	p	AIC	)	df	p
Sat	4055.93 f 1939.72 m	1767 900					χ^2		
Het	4059.21 f 1947.06 m	1770 903	3.28 7.33	3 3	.35 .06	-2.72 1.33			
Hom									

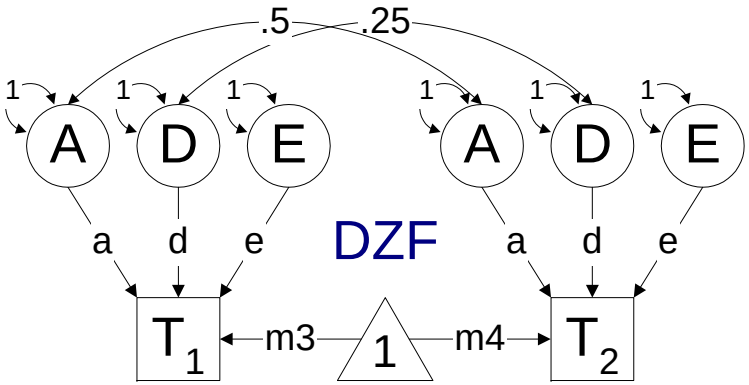
Goodness-of-Fit Statistics for BMI in young females+males

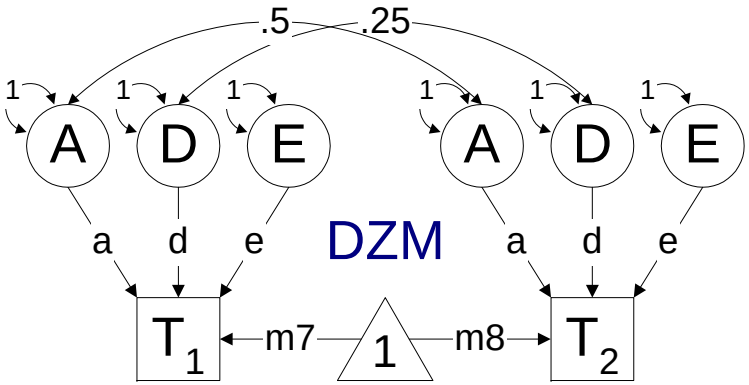
	-2LL	df	χ^2	df	p	AIC	)	df	p
Sat	4055.93 f 1939.72 m 5995.65	1767 900 2667					χ^2		
Het	4059.21 f 1947.06 m 6006.27	1770 903 2673	3.28 7.33 10.61	3 3 6	.35 .06 .10	-2.72 1.33 -1.39			
Hom									

Homogeneity









Exercise II

- Run Homogeneity model
  - Equate $a_f=a_m$
  - Equate $e_f=e_m$
  - Equate $d_f=d_m$

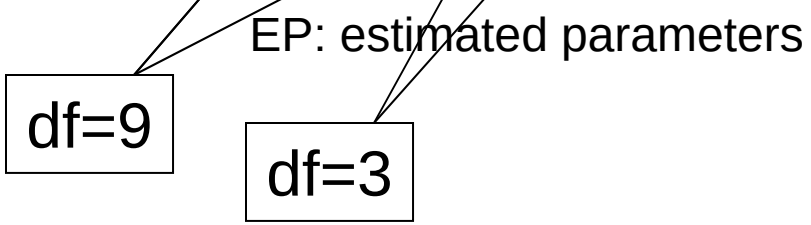
Homogeneity Script

- #NGroups 6
- G1: parameters
  - a, e, d
- G2: MZF data
  - m1, m2
- G3: DZF data
  - m3, m4
- G4: MZM data
  - m5, m6
- G5: DZM data
  - m7, m8
- G6: standardized estimates

ozbmiyade4eq.mx

Models for Concordant Pairs

	G1 MZ	G1 DZ	G2 MZ	G2 DZ	EP
Saturated	v1 v2 cov m1 m2	v3 v4 cov m3 m4	v5 v6 cov m5 m6	v7 v8 cov m7 m8	12 + 8
Heterogeneity	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_2 d_2 e_2 m5 m6	a_2 d_2 e_2 m7 m8	6 + 8
Homogeneity	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_1 d_1 e_1 m5 m6	a_1 d_1 e_1 m7 m8	3 + 8



Goodness-of-Fit Statistics for BMI in young females+males

	-2LL	df	χ^2	df	p	AIC	χ^2	df	p
Sat	4055.93 f 1939.72 m 5995.65	1767 900 2667							
Het	4059.21 f 1947.06 m 6006.27	1770 903 2673	3.28 7.33 10.61	3 3 6	.35 .06 .10	-2.72 1.33 -1.39			
Hom	6014.69	2676	19.03	9	.03	1.03	8.42	3	.04

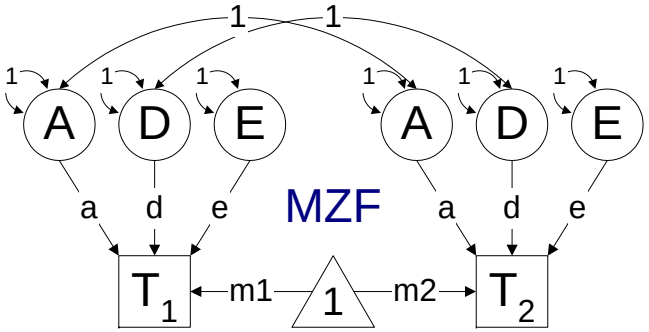
Parameter Estimates for BMI in young females+males

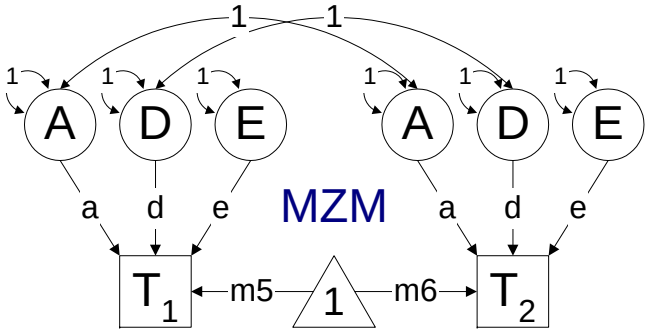
	females						males					
	Paths			Var Comp			Paths			Var Comp		
	a_f	e_f	d_f	a_f^2	e_f^2	d_f^2	a_m	e_m	d_m	a_m^2	e_m^2	d_m^2
Heterogeneity												
ADE	.56	.41	.54	.31	.17	.29	.49	.37	.54	.23	.14	.29
AE	.78	.42		.61	.17		.73	.38		.54	.14	
Homogeneity												
ADE	.54	.40	.54	.29	.16	.29	.54	.40	.54	.29	.16	.29
AE	.77	.40		.59	.16		.77	.40		.59	.16	

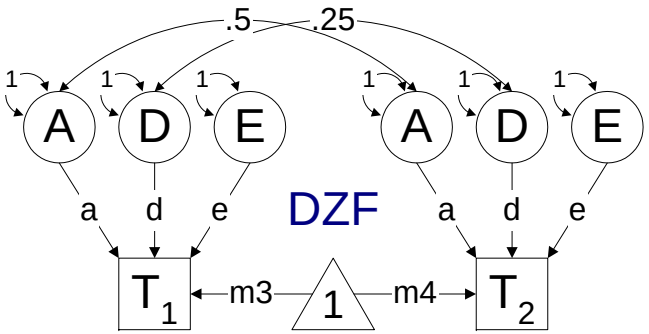
What about DZO?

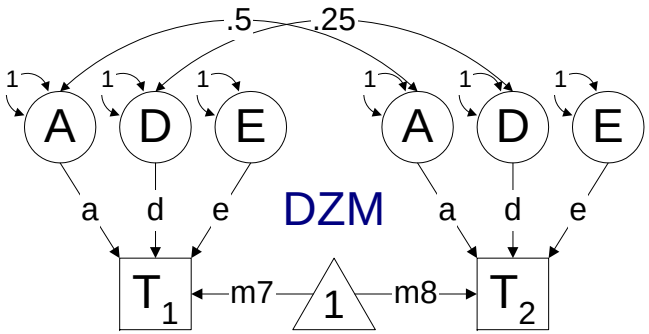
- Var F, Cov MZF, Cov DZF
  - a_f, d_f, e_f
- Var M, Cov MZM, Cov DZM
  - a_m, d_m, e_m
- Var Fdzo = Var F, Var M dzo = Var M
- Cov DZO
  - r_g

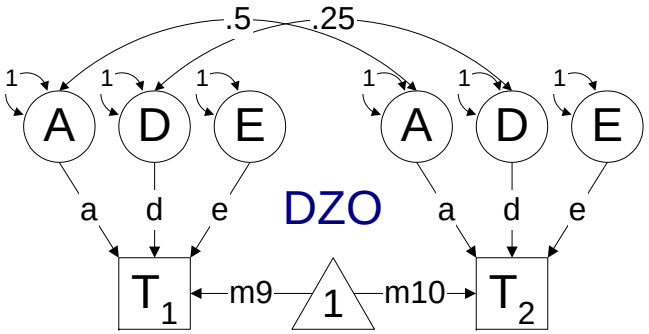
Homogeneity





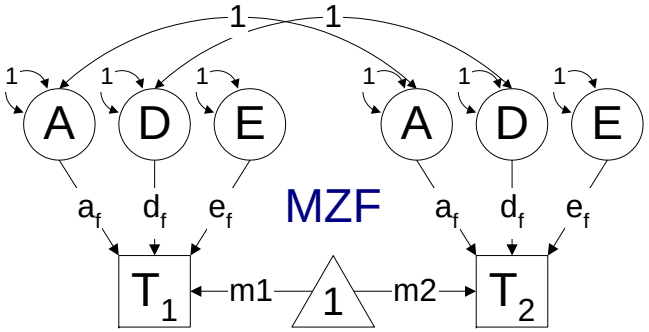


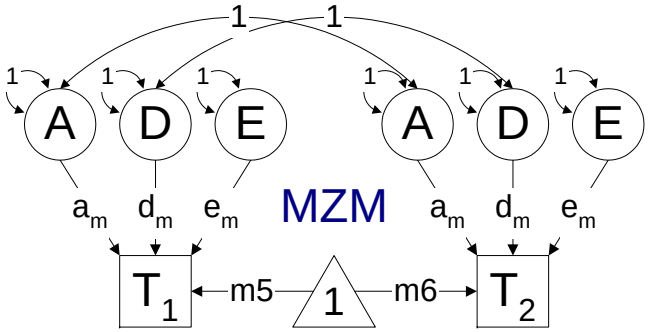


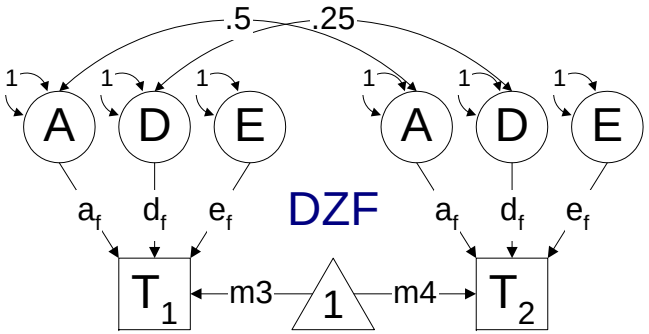


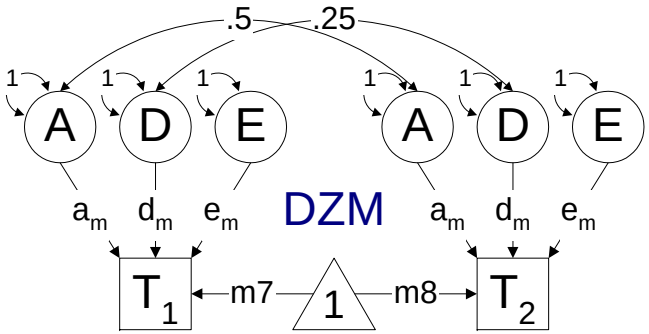
DZO	female	male
female	$a^2+e^2+d^2$	$.5a^2+.25d^2$
male	$.5a^2+.25d^2$	$a^2+e^2+d^2$

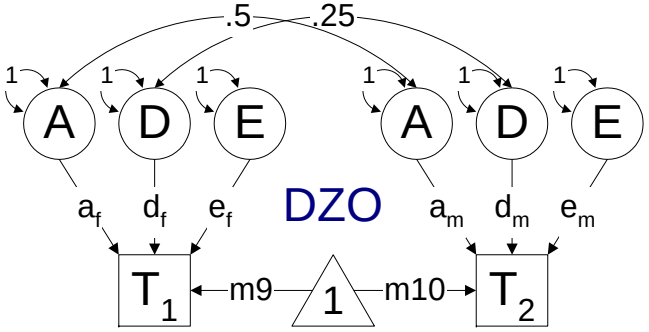
Heterogeneity





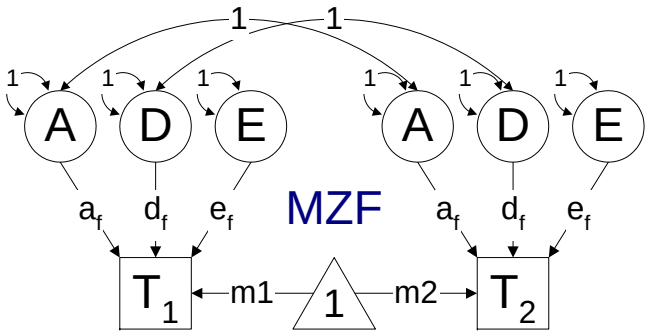


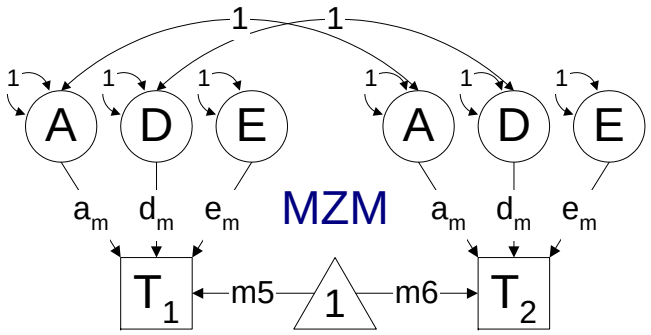


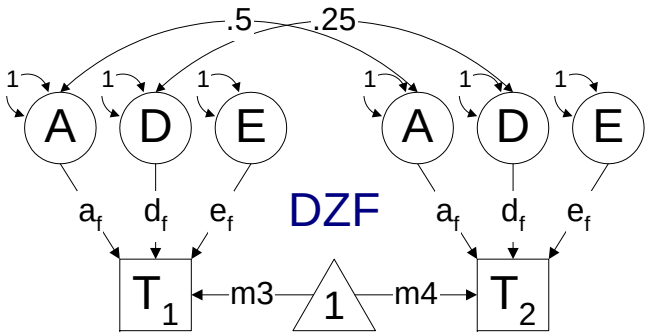


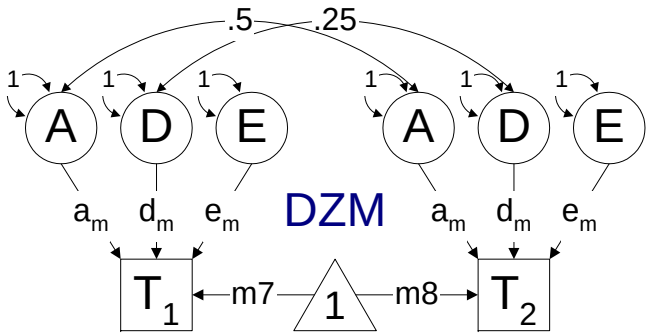
DZO	female	male
female	$a_f^2+e_f^2+d_f^2$	$.5a_fa_m'+.25d_fd_m'$
male	$.5a_ma_f'+.25d_md_f'$	$a_m^2+e_m^2+d_m^2$

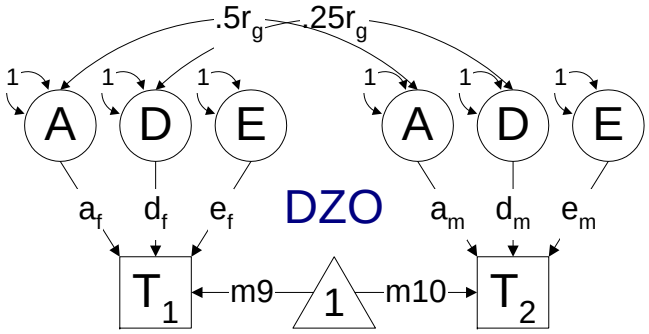
General Sex Limitation











DZO	female	male
female	$a_f^2+e_f^2+d_f^2$	$.5r_g a_f a_m' + .25r_g d_f d_m'$
male	$.5r_g a_m a_f' + .25r_g d_m d_f'$	$a_m^2+e_m^2+d_m^2$

Models for Concordant and Discordant Pairs

	G1 MZ	G1 DZ	G2 MZ	G2 DZ	G1G2 DZ	EP
Saturated	v1 v2 cov m1 m2	v3 v4 cov m3 m4	v5 v6 cov m5 m6	v7 v8 cov m7 m8	v9 v10 cov m9 m10	15 + 10
General	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_2 d_2 e_2 m5 m6	a_2 d_2 e_2 m7 m8	a_1 d_1 e_1 a_2 c_2 e_2 r_g m9 m10	7 + 10
Hetero-geneity	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_2 d_2 e_2 m5 m6	a_2 d_2 e_2 m7 m8	a_1 d_1 e_1 a_2 c_2 e_2 m9 m10	6 + 10
Homo-geneity	a_1 d_1 e_1 m1 m2	a_1 d_1 e_1 m3 m4	a_1 d_1 e_1 m5 m6	a_1 d_1 e_1 m7 m8	a_1 d_1 e_1 m9 m10	3 + 10

Exercise III

- Extend Saturated model to 5 groups
  - from ozbmiysat4.mx

Goodness-of-Fit Statistics for BMI in young females+males+DZO

-2LL	df	χ^2	df	p	AIC	$\Delta\chi^2$	df	p
Saturated								
General Sex Limitation								
Heterogeneity								
Homogeneity								

Goodness-of-Fit Statistics for BMI in young females+males+DZO

-2LL	df	χ^2	df	p	AIC	$\Delta\chi^2$	df	p
Saturated								
8310.31	3633							
General Sex Limitation								
Heterogeneity								
Homogeneity								

Summary of Models

- General Sex Limitation Model:
  - quantitative and qualitative differences
- Heterogeneity Model:
  - quantitative but no qualitative differences
- Homogeneity Model:
  - no quantitative, no qualitative differences

! Estimate variance components - ACED model
! OZ BMI data - young females & males + opp sex

```
#NGroups 7
#define nvar 1
#define nvar2 2

G1: Parameters
 Calculation
 Begin Matrices;
  X Lower nvar nvar Free  ! FEMALES a
  Y Lower nvar nvar       ! FEMALES c
  Z Lower nvar nvar Free  ! FEMALES e
  W Lower nvar nvar Free  ! FEMALES d
  S Lower nvar nvar Free  ! MALES a
  T Lower nvar nvar       ! MALES c
  U Lower nvar nvar Free  ! MALES e
  V Lower nvar nvar Free  ! MALES d
   H Full 1 1             ! scalar, 0.5
   Q Full 1 1             ! scalar, 0.25
  F Full 1 1 Free         ! free for DZO
 End Matrices;
```

Group 1 continued

```
Matrix H .5
 Matrix Q .25
 Start 1 F 1 1 1
 Bound 0 1 F 1 1 1
Begin Algebra;
 A= X*X';                    ! FEMALES a^2
 C= Y*Y';                    ! FEMALES c^2
 E= Z*Z';                    ! FEMALES e^2
 D= W*W';                    ! FEMALES d^2
 K= S*S';                    ! MALES a^2
 L= T*T';                    ! MALES c^2
 N= U*U';                    ! MALES e^2
 O= V*V';                    ! MALES d^2
End Algebra;
End
```

Groups 2 & 3

```
Title G2: MZf data
 #include ozbmi2.dat
 Select if zyg =1
 Select if agecat =1
 Select bmi1 bmi2 ;
 Begin Matrices = Group 1;
  M Full 1 nvar2 Free
 End Matrices;
 Means M;
 Covariance
    A+C+E+D | A+C+D   _
    A+C+D   | A+C+E+D;
 Option RSiduals;
End
```

```
Title G3: DZf data
 #include ozbmi2.dat
 Select if zyg =3
 Select if agecat =1
 Select bmi1 bmi2 ;
 Begin Matrices = Group 1;
  M Full 1 nvar2 Free
 End Matrices;
 Means M;
 Covariance
    A+C+E+D    | H@A+C+Q@D _
    H@A+C+Q@D  | A+C+E+D;
 Option RSiduals
End
```

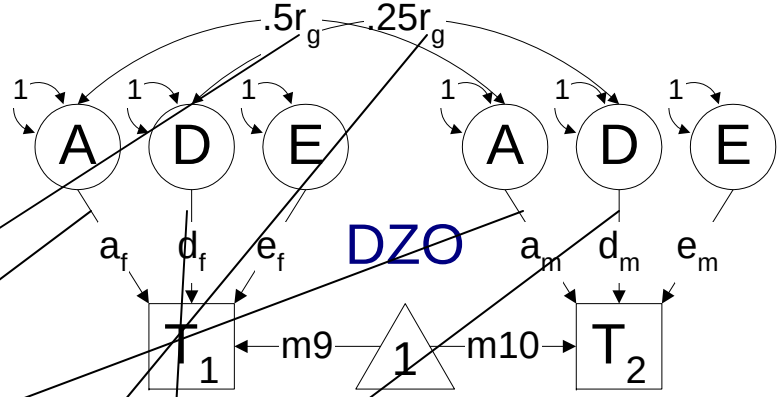
Groups 4 & 5

```
Title G4: MZm data
 #include ozbmi2.dat
 Select if zyg =2
 Select if agecat =1
 Select bmi1 bmi2 ;
 Begin Matrices = Group 1;
  M Full 1 nvar2 Free
 End Matrices;
 Means M;
 Covariance
    K+L+N+O | K+L+O   _
    K+L+O   | K+L+N+O  ;
 Option RSiduals;
End
```

```
Title G5: DZm data
 #include ozbmi2.dat
 Select if zyg =4
 Select if agecat =1
 Select bmi1 bmi2 ;
 Begin Matrices = Group 1;
  M Full 1 nvar2 Free
 End Matrices;
 Means M;
 Covariance
    K+L+N+O    | H@K+L+Q@O _
    H@K+L+Q@O | K+L+N+O  ;
 Option RSiduals
End
```

Group 6: DZO

```
Title G6: DZfm data
 #include ozbmi2.dat
 Select if zyg =5
 Select if agecat =1
 Select bmi1 bmi2 ;
 Begin Matrices = Group 1;
  M Full 1 nvar2 Free
 End Matrices;
 Means M;
 Covariance
    A+C+E+D    | F@H@(X*S')+(Y*T')+F@Q@(W*V') _
 F@H@(S*X')+(T*Y')+F@Q@(V*W')  | K+L+N+O  ;
 Option RSiduals
End
```



Variance females

Variance males

Group 7

```
Title G7: Standardization
 Calculation
 Begin Matrices = Group 1;
  Start .5 all
  Start 20 M 2 1 1 - M 2 1 nvar2
  Start 20 M 3 1 1 - M 3 1 nvar2
  Start 20 M 4 1 1 - M 4 1 nvar2
  Start 20 M 5 1 1 - M 5 1 nvar2
  Start 20 M 6 1 1 - M 6 1 nvar2
 Begin Algebra;
  G= A+C+E+D;                ! FEMALES total variance
  J= K+L+N+O;                ! MALES total variance
  P= A%G| C%G| E%G| D%G_     ! FEMALES stand variance components
     K%J| L%J| N%J| O%J;     ! MALES stand variance components
 End Algebra;
 Option NDecimals=4
!ADE model
 Option Sat=8310.308, 3633
 Option Multiple
End
```

Submodels

```
Last Group
 Option Sat=8310.308, 3633
 Option Multiple
End

 Option Issat
End

! Test for qualitative sex differences (nature of effect)
 Drop @1 F 1 1 1              ! drop rg
End

 Option Issat
End

! Test for quantitative sex differences (magnitude of effect)
 Equate X 1 1 1 S 1 1 1   ! a_f = a_m
 Equate Z 1 1 1 U 1 1 1   ! e_f = e_m
 Equate W 1 1 1 V 1 1 1   ! d_f = d_m
End
```

Exercise IV

- Run Sex Limitation Model on 5 groups
  - ozbmiyade5.mx

Parameter Estimates for BMI in young females+males+DZO

	females						males					
	Paths			Var Comp			Paths			Var Comp		
r_g	a_f	e_f	d_f	a_f^2	e_f^2	d_f^2	a_m	e_m	d_m	a_m^2	e_m^2	d_m^2
General Sex Limitation												
Heterogeneity												
Homogeneity												

Parameter Estimates for BMI in young females+males+DZO

	females						males					
	Paths			Var Comp			Paths			Var Comp		
r_g	a_f	e_f	d_f	a_f^2	e_f^2	d_f^2	a_m	e_m	d_m	a_m^2	e_m^2	d_m^2
General Sex Limitation												
Heterogeneity												
Homogeneity												

Goodness-of-Fit Statistics for BMI in young females+males+DZO

-2LL	df	χ^2	df	p	AIC	$\Delta\chi^2$	df	p
Saturated								
8310.31	3633							
General Sex Limitation								
8324.49	3641	14.18	8	.08	-1.82			
Heterogeneity								
8324.88	3642	14.57	9	.10	-3.43	.39	1	.53
Homogeneity								
8335.32	3645	25.01	12	.02	1.01	10.44	3	.02

Parameter Estimates for BMI in young females+males+DZO

	females						males					
	Paths			Var Comp			Paths			Var Comp		
r_g	a_f	e_f	d_f	a_f^2	e_f^2	d_f^2	a_m	e_m	d_m	a_m^2	e_m^2	d_m^2
General Sex Limitation												
.87	.53	.41	.55	.28	.17	.30	.47	.37	.54	.22	.14	.29
Heterogeneity												
1.00	.52	.41	.56	.27	.17	.31	.39	.37	.60	.15	.14	.36
Homogeneity												
1.00	.47	.40	.58	.22	.16	.33	.47	.40	.58	.22	.16	.33