

# **Liability Threshold Models**

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**Twin Workshop, Boulder**

**Tuesday March 4<sup>th</sup> 2008**

# Aims

- Introduce model fitting to categorical data
  - Define liability and describe assumptions of the liability model
  - Show how heritability of liability can be estimated from categorical twin data
- Selection
- Practical exercise

# Ordinal data

**Measuring instrument  
discriminates between two or  
a few ordered categories**

- Absence (0) or presence (1) of a disorder
- Score on a Q item e.g. : 0 - 1, 0 - 4

# **A single ordinal variable**

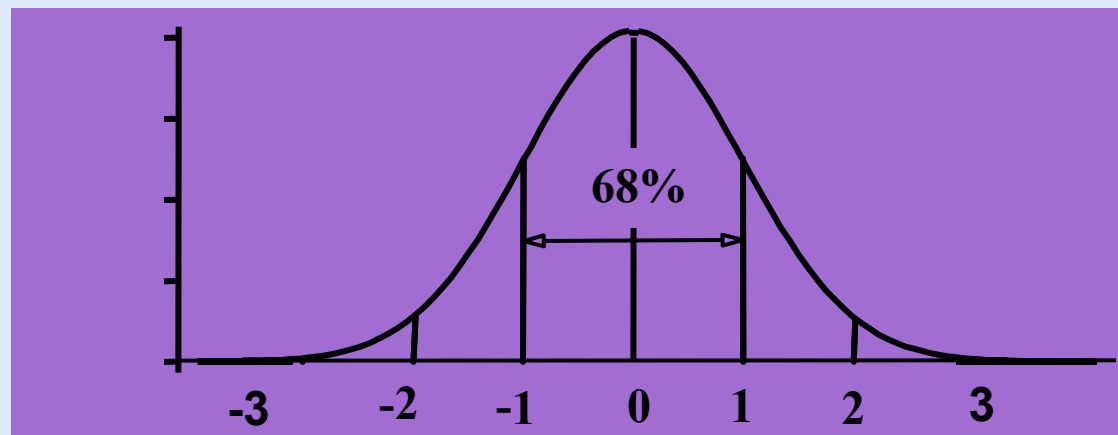
## **Assumptions:**

- (1) Underlying normal distribution of liability**
- (2) The liability distribution has 1 or more thresholds (cut-offs)**

# The standard Normal distribution

Liability is a *latent* variable, the scale is arbitrary, distribution is, therefore, assumed to be the *Standard Normal Distribution (SND)* or z-distribution:

- mean ( $\mu$ ) = 0 and SD ( $\sigma$ ) = 1
- z-values are the number of SD away from the mean
- area under curve translates directly to probabilities  
> Stand Normal Probability Density function ( $\Phi$ )

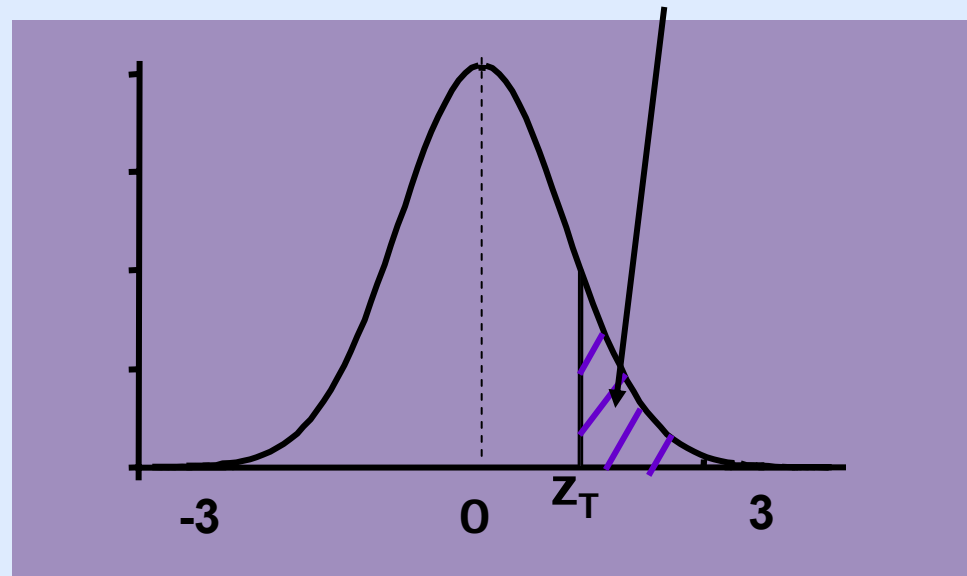


# Standard Normal Cumulative Probability in right-hand tail

(For negative z values, areas are found by symmetry)

$Z_0$	Area	
0	.50	50%
.2	.42	42%
.4	.35	35%
.6	.27	27%
.8	.21	21%
1	.16	16%
1.2	.12	12%
1.4	.08	8%
1.6	.06	6%
1.8	.036	3.6%
2	.023	2.3%
2.2	.014	1.4%
2.4	.008	.8%
2.6	.005	.5%
2.8	.003	.3%
2.9	.002	.2%

$$\text{Area} = P(z \geq z_T)$$

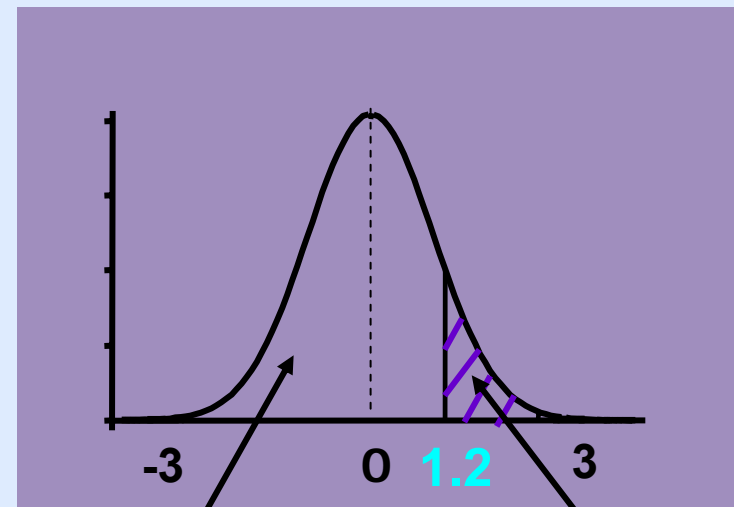


$$\int_{z_T}^{\infty} \Phi(L_1; \mu = 0, \sigma^2 = 1) dL_1$$

## Example: single dichotomous variable

It is possible to find a **z-value** (threshold) so that the proportion exactly matches the observed proportion of the sample  
e.g. sample of **1000** individuals, where **120** have met the criteria for a disorder (**12%**): the z-value is **1.2**

$Z_0$	Area	
.6	.27	27%
.8	.21	21%
1	.16	16%
1.2	.12	12%
1.4	.08	8%
1.6	.055	6%
1.8	.036	3.6%
2	.023	2.3%
2.2	.014	1.4%
2.4	.008	.8%
2.6	.005	.5%
2.8	.003	.3%
2.9	.002	.2%



Unaffected (0)

Affected (1)

Counts: 880

120

# Two ordinal variables: Data from twin pairs

> Contingency Table with 4 observed cells:

cell **a**: pairs concordant for unaffected

cell **d**: pairs concordant for affected

cell **b/c**: pairs discordant for the disorder

Twin1 Twin2	0	1
0	<b>a</b>	<b>b</b>
1	<b>c</b>	<b>d</b>

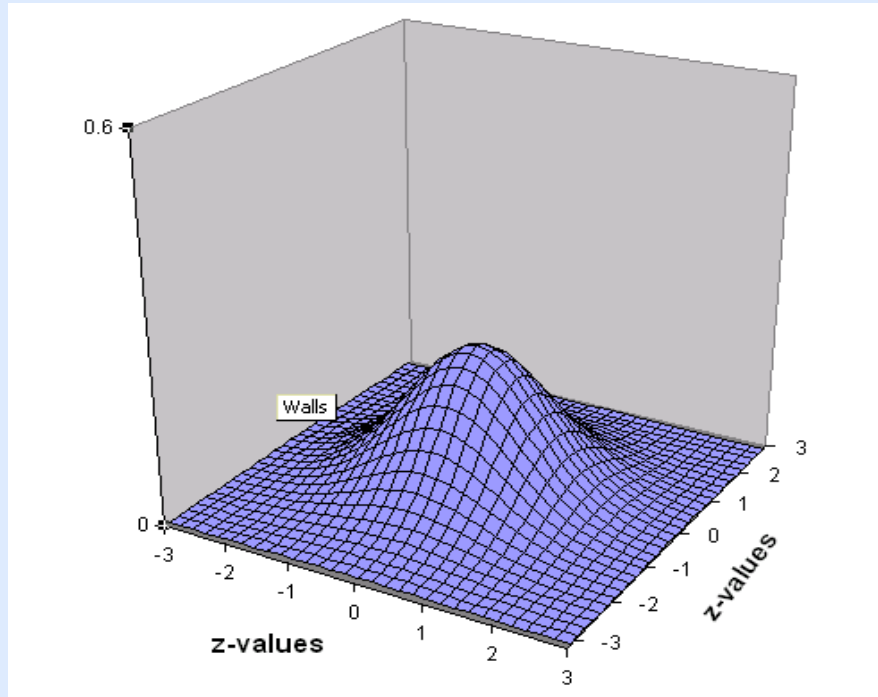
**0 = unaffected**  
**1 = affected**



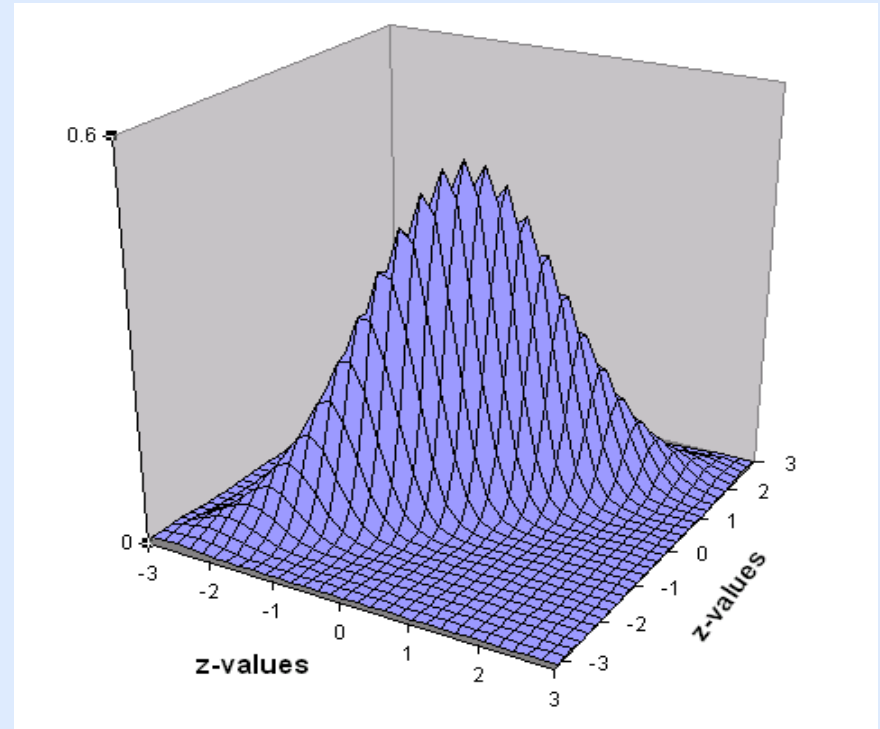
# Joint Liability Model for twin pairs

- Assumed to follow a **bivariate normal** distribution, where both traits have a mean of 0 and standard deviation of 1, but the **correlation** between them is unknown.
- The **shape** of a bivariate normal distribution is determined by the **correlation** between the traits

# Bivariate Normal

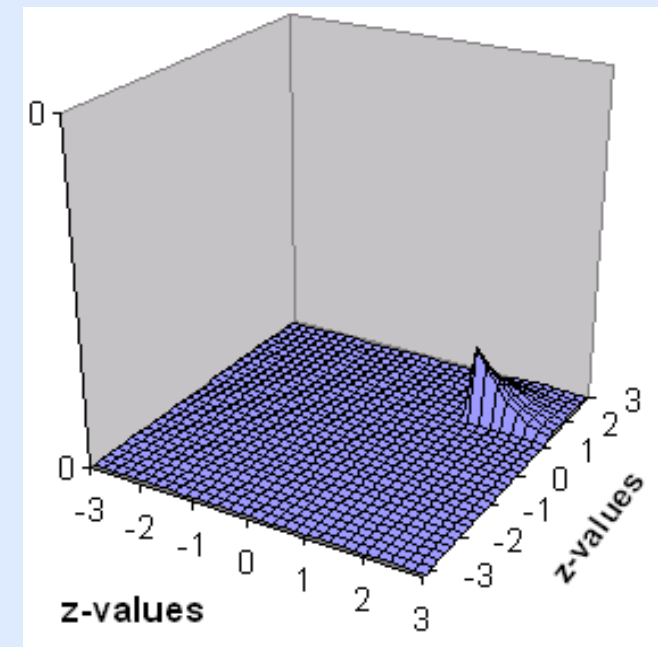
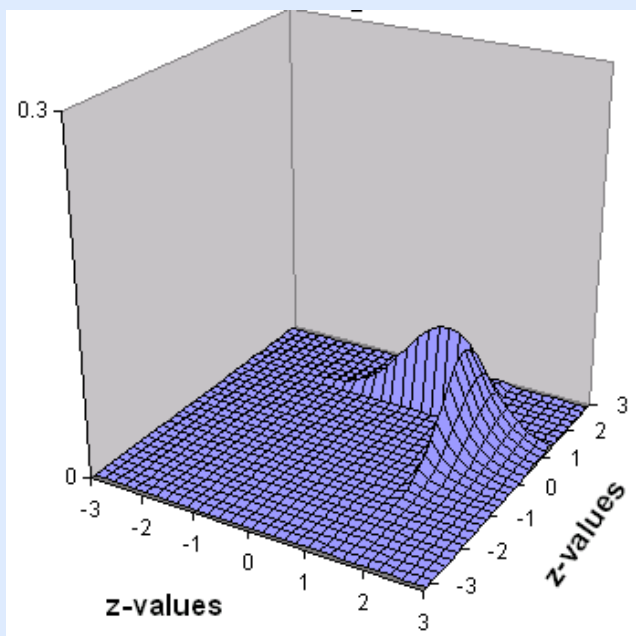
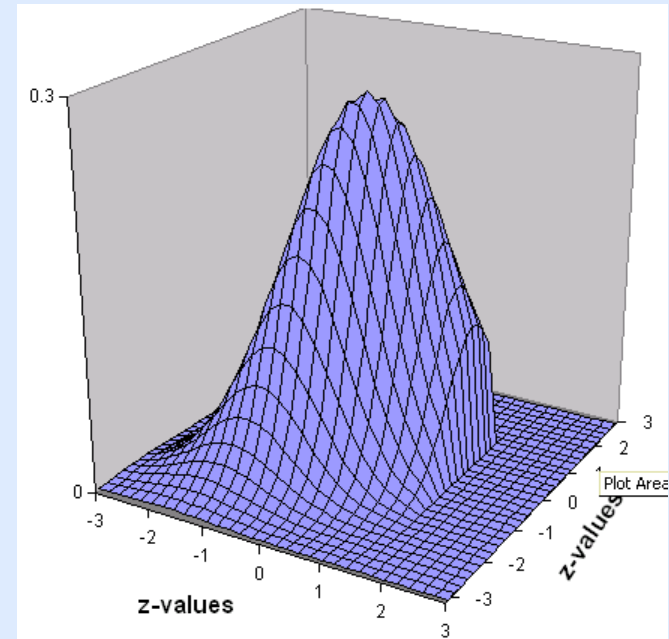
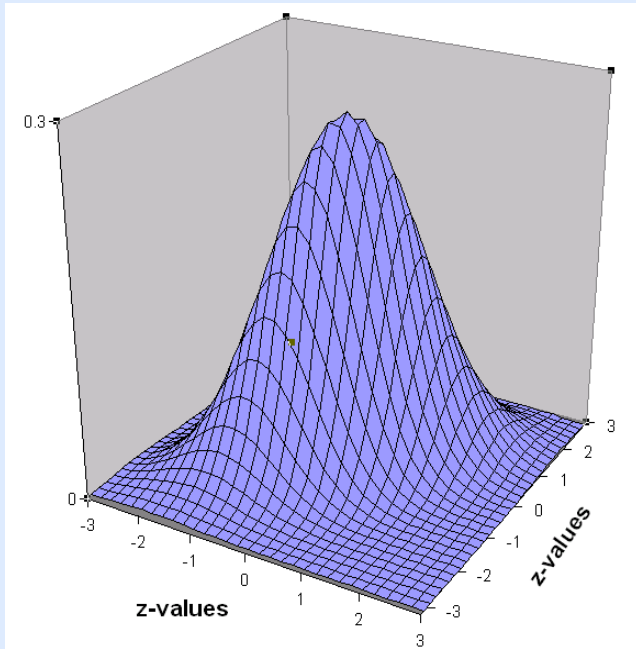


$$r = .00$$



$$r = .90$$

# Bivariate Normal ( $R=0.6$ ) partitioned at threshold 1.4 (z-value) on both liabilities



# Expected proportions

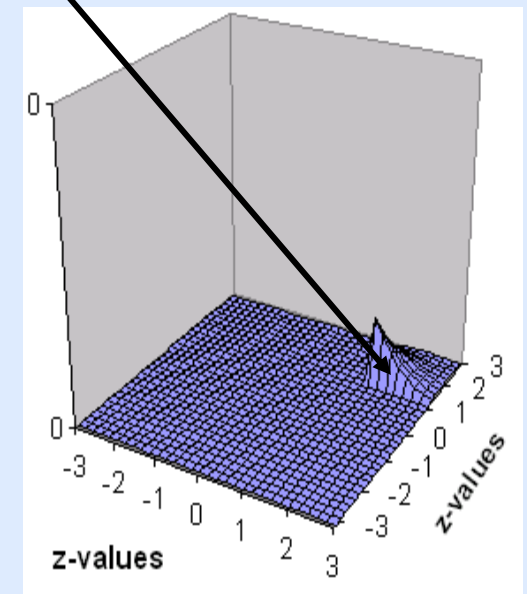
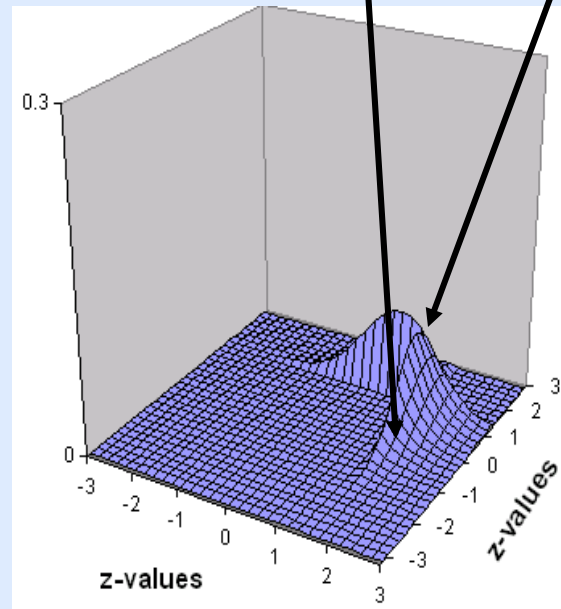
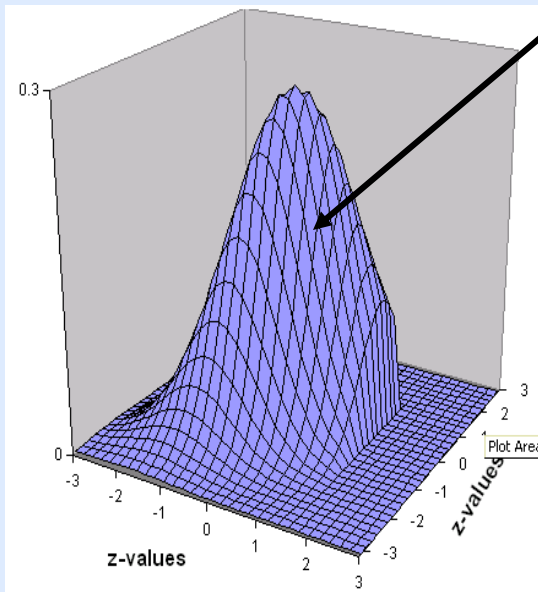
By **numerical integration** of the bivariate normal over two dimensions: the liabilities for twin1 and twin2  
e.g. the probability that both twins are affected :

$$\int_{T_1}^{\infty} \int_{T_2}^{\infty} \Phi(L_1, L_2; \mathbf{0}, \Sigma) dL_1 dL_2$$

**$\Phi$**  is the bivariate normal probability density function,  
 **$L_1$**  and  **$L_2$**  are the liabilities of twin1 and twin2, with means  **$\mathbf{0}$** ,  
and  **$\Sigma$**  is the correlation matrix of the two liabilities  
 **$T_1$**  is threshold (z-value) on  **$L_1$** ,  **$T_2$**  is threshold (z-value) on  **$L_2$**

# Expected Proportions of the BN, for $R = 0.6$ , $T_1 = 1.4$ , $T_2 = 1.4$

		Liab 2	
		0	1
Liab 1	0	.87	.05
	1	.05	.03

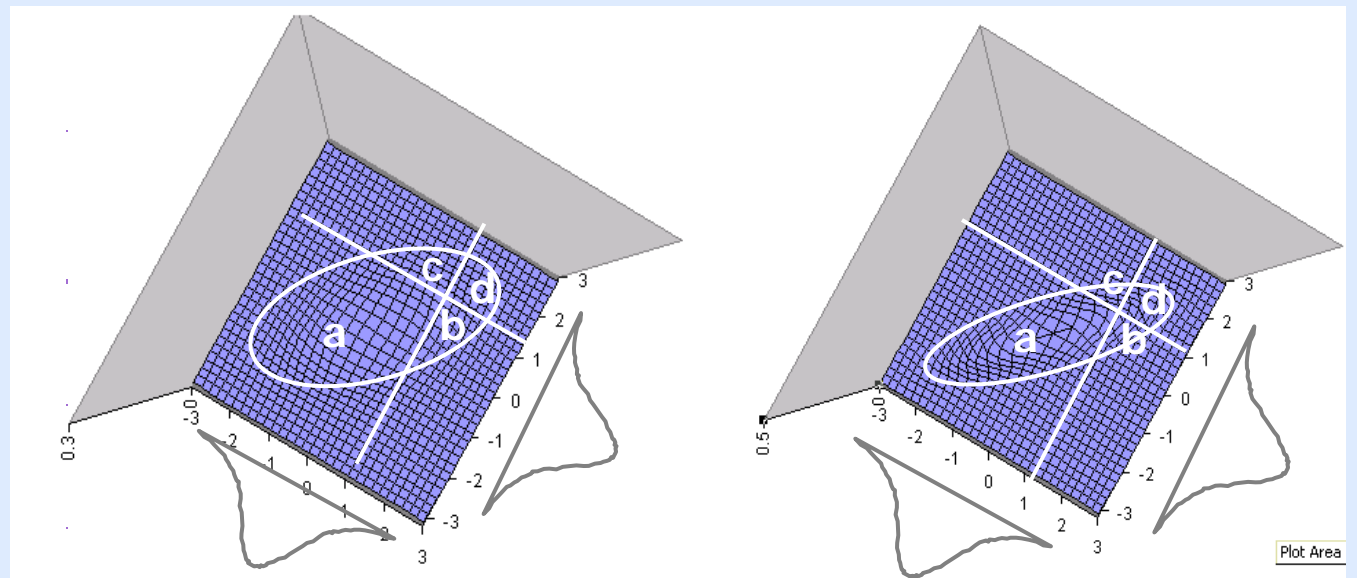


# How can we estimate correlations from CT?

The correlation (shape) of the BN and the two thresholds determine the relative proportions of observations in the 4 cells of the CT.

Conversely, the sample proportions in the 4 cells can be used to estimate the correlation and the thresholds.

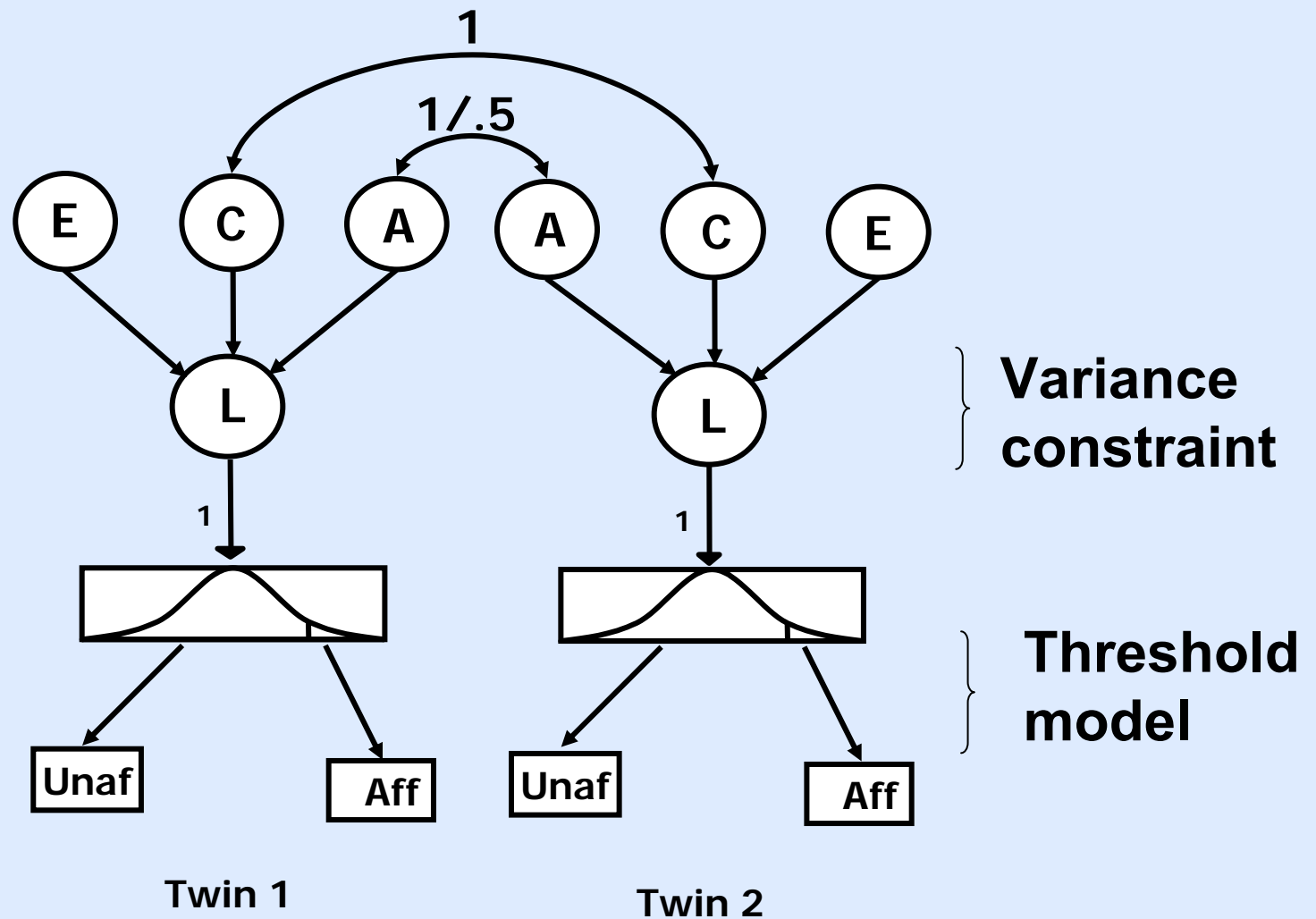
Twin2 Twin1	0	1
0	a	b
1	c	d



# The classical Twin Model

- Estimate correlation in liability separately for MZ and DZ
  - A variance decomposition (A, C, E) can be applied to *liabilities*
- estimate of the heritability of the *liability*

# ACE Liability Model





# Summary

- To estimate correlations for categorical traits (counts) we make assumptions about the joint distribution of the data (Bivariate Normal)
- The relative proportions of observations in the cells of the Contingency Table are translated into proportions under the BN
- The most likely thresholds and correlations are estimated
- Genetic/Environmental variance components are estimated based on these correlations derived from MZ and DZ data

# How can we fit ordinal data in Mx?

## 1. Summary statistics: CT

Mx has a built-in fit function for the maximum likelihood analysis of 2-way Contingency Tables

> analyses limited to only **two** variables, with 2 or more ordered classes

Tetrachoric

Polychoric

CTable 2 2

40 5

4 10

CT 3 3

39 4 5

6 15 6

4 7 10

CT 3 2

39 13

16 15

14 20

} **Mx input lines**

# Fit function

1. Mx calculates twice the log-likelihood of the observed frequency data under the model using:
  - Observed frequency in each cell
  - Expected proportion in each cell (Num Integration of the BN)
2. Mx calculates the log-likelihood of the observed frequency data themselves
3. An approximate  $\chi^2$  statistic is then computed by taking the differences in these 2 likelihoods

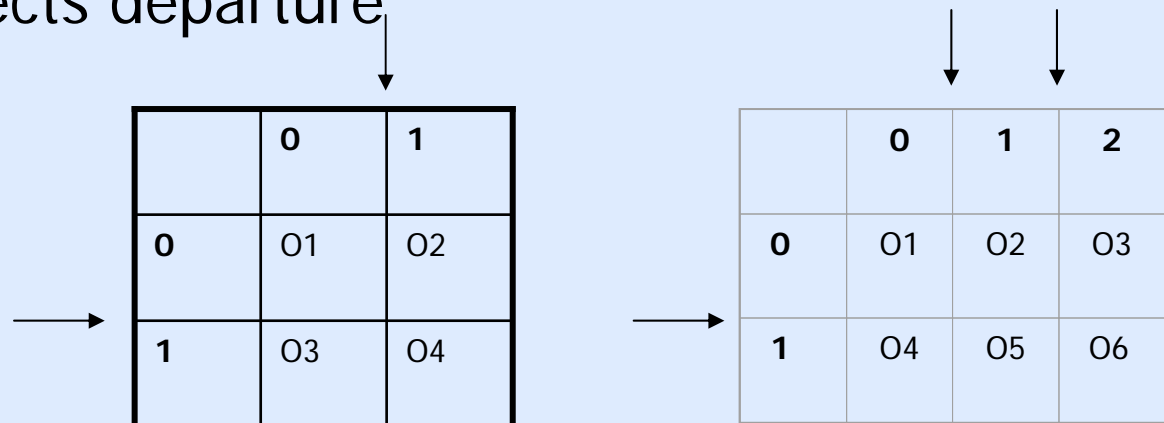
(Equations given in Mx manual, pg 91-92)

## Test of assumption

For a 2x2 CT with 1 estimated TH on each liability, the  $\chi^2$  statistic is always 0, 3 observed statistics, 3 param, df=0 (it is always possible to find a correlation and 2 TH to perfectly explain the proportions in each cell). No goodness of fit of the normal distribution assumption.

This problem is resolved if the CT is at least 2x3 (i.e. more than 2 categories on at least one liability)

A significant  $\chi^2$  reflects departure from normality.



# How can we fit ordinal data in Mx?

## 2. Raw data analyses

- Advantages over CT:
  - multivariate
  - handles missing data
  - moderator variables  
(for covariates e.g. age)

ORD File=...dat

}

Mx input lines

# Fit function

- The likelihood for a vector of observed ordinal responses is computed by the expected proportion in the corresponding cell of the MV distribution
- The likelihood of the model is the sum of the likelihoods of all vectors of observation
- This is a value that depends on the number of observations and isn't very interpretable (as with continuous data)
- So we compare it with the LL of other models, or a saturated (correlation) model to get a  $\chi^2$  model-fit index

(Equations given in Mx manual, pg 89-90)

# Raw Ordinal Data File

Zyg	ordinal respons1	ordinal respons2
1	0	0
1	0	0
1	0	1
2	1	0
2	0	0
1	1	1
2	.	1
2	0	.
2	0	1

**NOTE: smallest category should always be 0 !!**

# SORT !

- Sorting speeds up computation time  
If  $i = i+1$  then likelihood not recalculated

In e.g. bivariate, 2 category case, there are only 4 possible vectors of observations:

1 1, 0 1, 1 0, 00

and, therefore, only 4 integrals for  $Mx$  to calculate if the data file is sorted.



# Selection

# Selection

For rare disorders (e.g. Schizophrenia), selecting a random population sample of twins will lead to the vast majority of pairs being unaffected.

A more efficient design is to ascertain twin pairs through a register of affected individuals.

# Types of ascertainment

## Double (complete) Ascertainment

Twins Twin 1 Twin 2	0	1
0	00 <sup>a</sup>	01 <sup>b</sup>
1	10 <sup>c</sup>	11 <sup>d</sup>

## Single Ascertainment

Proband Co-twin	0	1
0	00 <sup>a</sup>	01 <sup>b</sup>
1	10 <sup>c</sup>	11 <sup>d</sup>

# Ascertainment Correction

**When using ascertained samples, the Likelihood Function needs to be corrected.**

Omission of certain classes from observation leads to an increase of the likelihood of observing the remaining individuals

Need re-normalization

Mx corrects for incomplete ascertainment by dividing the likelihood by the proportion of the population remaining after ascertainment

# Ascertainment Correction in Mx: univariate

**Complete  
Ascertainment**

**CTable 2 2**

<b>-1</b>	<b>b</b>
<b>c</b>	<b>d</b>

**Single  
Ascertainment**

**CTable 2 2**

<b>-1</b>	<b>b</b>
<b>-1</b>	<b>d</b>

CT from ascertained data can be analysed in Mx by simply substituting a **-1** for the missing cells

- Thresholds need to be fixed > population prevalence of disorder e.g. Schiz (1%), z-value = 2.33

# Ascertainment Correction in Mx: multivariate

Write own fit function.

Adjustment of the Likelihood function is accomplished by specifying a user-defined fit function that adjusts for the missing cells (proportions) of the distribution.

**A twin study of genetic relationships between psychotic symptoms.  
Cardno, Rijdsdijk, Sham, Murray, McGuffin, Am J Psychiatry.  
2002, 159(4):539-45**

**Practical**

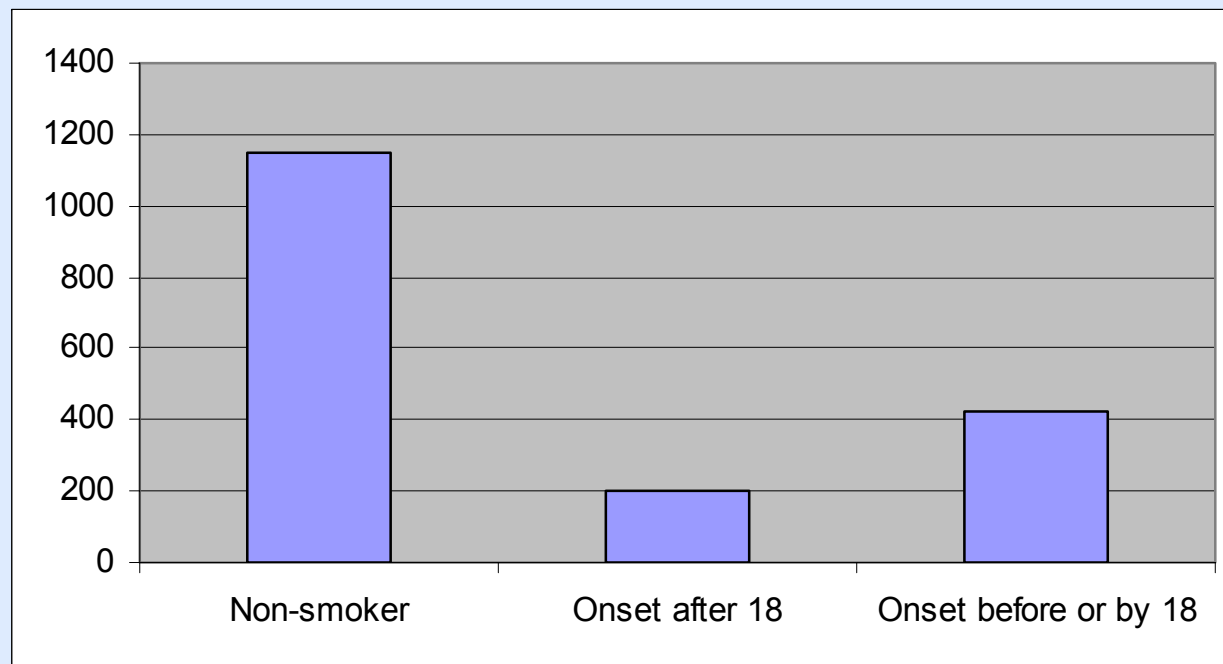
# Sample and Measures

- Australian Twin Registry data (QIMR)
- Self-report questionnaire
  - Non-smoker, ex-smoker, current smoker
  - Age of smoking onset
- Large sample of adult twins  
+ family members
  - Today using MZMs (785 pairs)  
and DZMs (536 pairs)





- Variable: age at smoking onset, including non-smokers
- Ordered as:
  - Non-smokers / late onset / early onset



# Practical Exercise

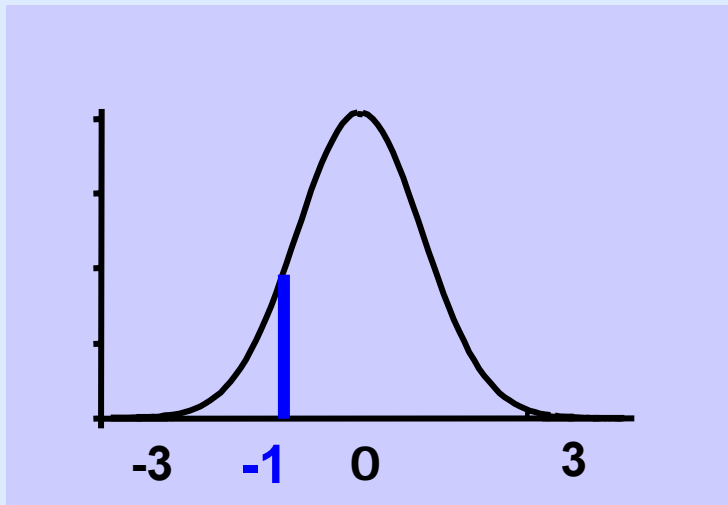
## Analysis of age of onset data

- Estimate thresholds
- Estimate correlations
- Fit univariate model

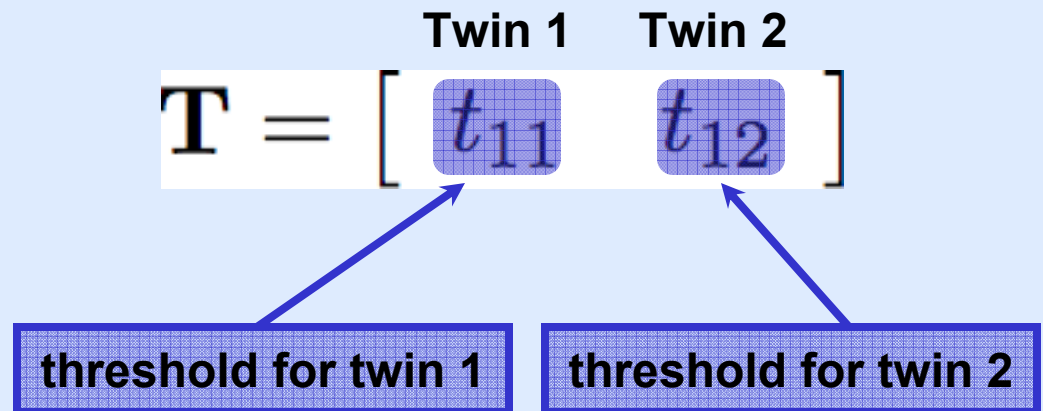
Observed counts from ATR data:

		MZM					DZM		
		Twin 1					Twin 1		
		0	1	2			0	1	2
Twin 2	0	368	24	46	Twin 2	0	203	22	63
	1	26	15	21		1	17	5	16
	2	54	22	209		2	65	12	133

# Mx Threshold Specification: Binary

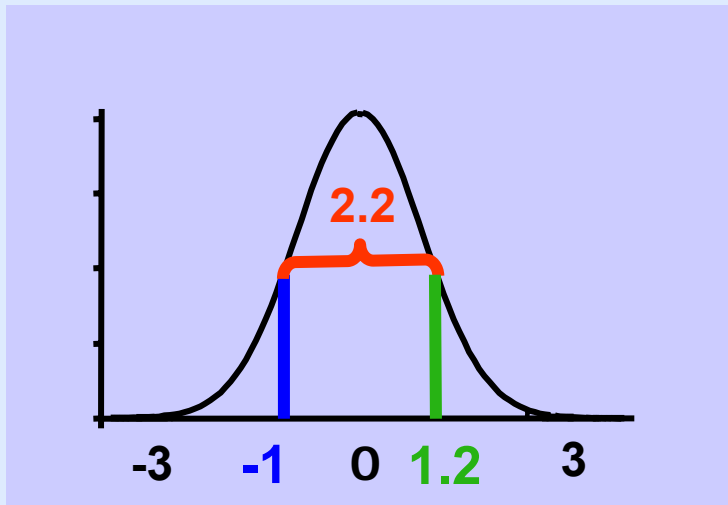


Threshold matrix: T Full 1 2 Free



Mx Threshold Model: Thresholds T /

# Mx Threshold Specification: 3+ Cat.



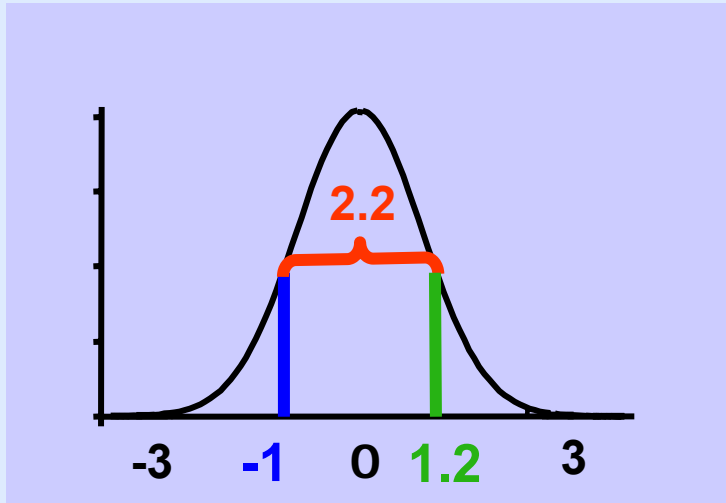
Threshold matrix: T Full 2 2 Free

$$\mathbf{T} = \begin{array}{c} \text{Twin 1} \quad \text{Twin 2} \\ \left[ \begin{array}{cc} t_{11} & t_{12} \\ t_{21} & t_{22} \end{array} \right] \end{array}$$

1st threshold

increment

# Mx Threshold Specification: 3+ Cat.



Threshold matrix: T Full 2 2 Free

$$\mathbf{T} = \begin{array}{c} \text{Twin 1} \quad \text{Twin 2} \\ \left[ \begin{array}{cc} t_{11} & t_{12} \\ t_{21} & t_{22} \end{array} \right] \end{array}$$

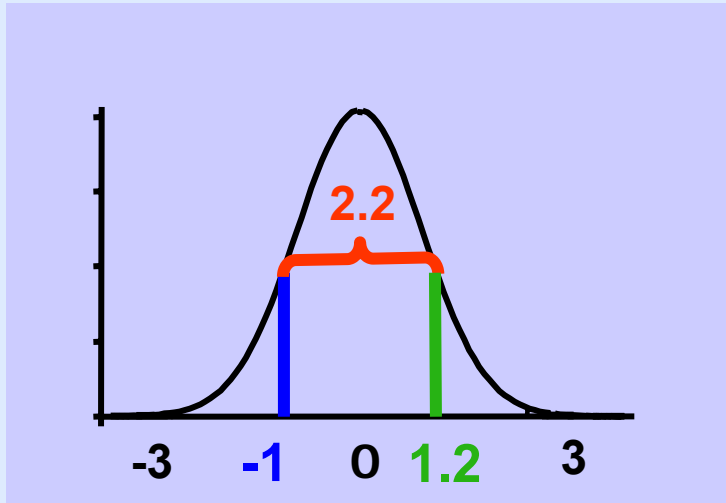
1st threshold
increment

Mx Threshold Model: Thresholds  $L * T /$

$$L * T = \begin{bmatrix} 1 & 0 \\ 1 & 1 \end{bmatrix} * \begin{bmatrix} t_{11} & t_{12} \\ t_{21} & t_{22} \end{bmatrix}$$

$$= \begin{bmatrix} t_{11} & t_{12} \\ t_{11} + t_{21} & t_{12} + t_{22} \end{bmatrix}$$

# Mx Threshold Specification: 3+ Cat.



Threshold matrix: T Full 2 2 Free

$$\mathbf{T} = \begin{matrix} & \text{Twin 1} & \text{Twin 2} \\ \begin{bmatrix} t_{11} & t_{12} \\ t_{21} & t_{22} \end{bmatrix} \end{matrix}$$

1st threshold

increment

Mx Threshold Model: Thresholds  $L * T /$

$$L * T = \begin{bmatrix} 1 & 0 \\ 1 & 1 \end{bmatrix} * \begin{bmatrix} t_{11} & t_{12} \\ t_{21} & t_{22} \end{bmatrix}$$

$$= \begin{bmatrix} t_{11} & t_{12} \\ t_{11} + t_{21} & t_{12} + t_{22} \end{bmatrix}$$

2nd threshold

# polycor\_smk.mx

```
#define nvarx2 2
#define nthresh 2
#ngroups 2

G1: Data and model for MZM correlation
Data NInput_vars=3
Missing=.
Ordinal File=smk_prac.ord
Labels
    zyg ageon_t1 ageon_t2
SELECT IF zyg = 2
SELECT ageon_t1 ageon_t2 /

Begin Matrices;
R STAN nvarx2 nvarx2 FREE
T FULL nthresh nvarx2 FREE
L Lower nthresh nthresh
End matrices;

Value 1 L 1 1 to L nthresh nthresh
```

# polycor\_smk.mx

```
#define nvarx2 2      ! Number of variables x number of twins
#define nthresh 2    ! Number of thresholds=num of cat-1
#ngroups 2
```

```
G1: Data and model for MZM correlation
```

```
Data NInput_vars=3
```

```
Missing=.
```

```
Ordinal File=smk_prac.ord ! Ordinal data file
```

```
Labels
```

```
zyg ageon_t1 ageon_t2
```

```
SELECT IF zyg = 2
```

```
SELECT ageon_t1 ageon_t2 /
```

```
Begin Matrices;
```

```
R STAN nvarx2 nvarx2 FREE
```

```
T FULL nthresh nvarx2 FREE
```

```
L Lower nthresh nthresh
```

```
End matrices;
```

```
Value 1 L 1 1 to L nthresh nthresh
```



# polycor\_smk.mx

```
#define nvarx2 2          ! Number of variables per pair
#define nthresh 2        ! Number of thresholds=num of cat-1
#ngroups 2
```

```
G1: Data and model for MZM correlation
```

```
Data NInput_vars=3
```

```
Missing=.
```

```
Ordinal File=smk_prac.ord ! Ordinal data file
```

```
Labels
```

```
zyg ageon_t1 ageon_t2
```

```
SELECT IF zyg = 2
```

```
SELECT ageon_t1 ageon_t2 /
```

```
Begin Matrices;
```

```
R STAN nvarx2 nvarx2 FREE ! Correlation matrix
```

```
T FULL nthresh nvarx2 FREE
```

```
L Lower nthresh nthresh
```

```
End matrices;
```

```
Value 1 L 1 1 to L nthresh nthresh
```

# polycor\_smk.mx

```
#define nvarx2 2          ! Number of variables per pair
#define nthresh 2        ! Number of thresholds=num of cat-1
#ngroups 2
```

```
G1: Data and model for MZM correlation
```

```
Data NInput_vars=3
```

```
Missing=.
```

```
Ordinal File=smk_prac.ord ! Ordinal data file
```

```
Labels
```

```
zyg ageon_t1 ageon_t2
```

```
SELECT IF zyg = 2
```

```
SELECT ageon_t1 ageon_t2 /
```

```
Begin Matrices;
```

```
R STAN nvarx2 nvarx2 FREE ! Correlation matrix
```

```
T FULL nthresh nvarx2 FREE ! thresh tw1, thresh tw2
```

```
L Lower nthresh nthresh ! Sums threshold increments
```

```
End matrices;
```

```
Value 1 L 1 1 to L nthresh nthresh ! initialize L
```

COV                    R /

Thresholds        L\*T /

Bound 0.01 1 T 1 1 T 1 2

Bound 0.1 5 T 2 1 T 2 2

Start 0.2 T 1 1 T 1 2

Start 0.2 T 2 1 T 2 2

Start .6 R 2 1

Option RS

Option func=1.E-10

END

COV                    R /        ! Predicted Correlation matrix for MZ pairs

Thresholds        L\*T /        ! Threshold model, to ensure t1>t2>t3 etc.

Bound 0.01 1 T 1 1 T 1 2

Bound 0.1 5 T 2 1 T 2 2

Start 0.2 T 1 1 T 1 2

Start 0.2 T 2 1 T 2 2

Start .6 R 2 1

Option RS

Option func=1.E-10

END

```
COV          R /      ! Predicted Correlation matrix for MZ pairs
```

```
Thresholds  L*T /    ! Threshold model, to ensure t1>t2>t3 etc.
```

```
Bound 0.01 1 T 1 1 T 1 2
```

```
Bound 0.1 5 T 2 1 T 2 2      !Ensures +ve threshold increment
```

```
Start 0.2 T 1 1 T 1 2      !Starting value for 1st thresholds
```

```
Start 0.2 T 2 1 T 2 2      !Starting value for increment
```

```
Start .6 R 2 1              !Starting value for correlation
```

```
Option RS
```

```
Option func=1.E-10      !Function precision less than usual
```

```
END
```

```
! Test equality of thresholds between Twin 1 and Twin 2
EQ T 1 1 1 T 1 1 2 !constrain TH1 equal across Tw1 and Tw2 MZM
EQ T 1 2 1 T 1 2 2 !constrain TH2 equal across Tw1 and Tw2 MZM
EQ T 2 1 1 T 2 1 2 !constrain TH1 equal across Tw1 and Tw2 DZM
EQ T 2 2 1 T 2 2 2 !constrain TH2 equal across Tw1 and Tw2 DZM
End
```

Get cor.mxs

```
! Test equality of thresholds between MZM & DZM
EQ T 1 1 1 T 1 1 2 T 2 1 1 T 2 1 2 !TH1 equal across all males
EQ T 1 2 1 T 1 2 2 T 2 2 1 T 2 2 2 !TH2 equal across all males
End
```

# Estimates: Saturated Model

-2LL	df			Twin 1	Twin 2		Twin 1	Twin 2
Saturated				MZ		DZ		
5128.185	3055		Threshold 1	0.09	0.12		0.03	0.05
			Threshold 2	0.31	0.33		0.24	0.26
			Correlation	0.81			0.55	

**MATRIX R:**

	1	2
1	1.0000	
2	0.8095	1.0000

**MATRIX T:**

	1	2
1	0.0865	0.1171
2	0.2212	0.2153

**Matrix of EXPECTED thresholds**

		AGEON_T1	AGEON_T2
Threshold 1	1	0.0865	0.1171
Threshold 2	2	0.3078	0.3324

# Estimates: Saturated Model

-2LL	df			Twin 1	Twin 2		Twin 1	Twin 2
Saturated				MZ		DZ		
5128.185	3055		Threshold 1	0.09	0.12		0.03	0.05
			Threshold 2	0.31	0.33		0.24	0.26
			Correlation	0.81			0.55	

MATRIX R:

	1	2
1	1.0000	
2	0.8095	1.0000

MATRIX T:

	1	2
1	0.0865	0.1171
2	0.2212	0.2153

Matrix of EXPECTED thresholds

	AGEON_T1	AGEON_T2
Threshold 1	0.0865	0.1171
Threshold 2	0.3078	0.3324



# Exercise I

- Fit saturated model
  - Estimates of thresholds
  - Estimates of polychoric correlations
- Test equality of thresholds
  - Examine differences in threshold and correlation estimates for saturated model and sub-models
- Examine correlations
  - What model should we fit?

**Raw ORD File:** **smk\_prac.ord**

**Script:** **polychor\_smk.mx**

**Location:** **Faculty\Fruhling\Categorical\_Data**

# Estimates: Sub-models

$\chi^2$	df	P		Twin 1	Twin 2		Twin 1	Twin 2
Sub-model 1				MZ			DZ	
			Threshold 1					
			Threshold 2					
			Correlation					
Sub-model 2				MZ			DZ	
			Threshold 1					
			Threshold 2					
			Correlation					

Raw ORD File: **smk\_prac.ord**  
 Script: **polychor\_smk.mx**  
 Location: **Faculty\Fruhling\Categorical\_Data**

# Estimates: Sub-models

$\chi^2$	df	P		Twin 1	Twin 2		Twin 1	Twin 2
Sub-model 1				MZ			DZ	
0.77	4	0.94	Threshold 1	0.10	0.10		0.04	0.04
			Threshold 2	0.32	0.32		0.25	0.25
			Correlation	0.81			0.55	
Sub-model 2				MZ			DZ	
2.44	6	0.88	Threshold 1	0.07	0.07		0.07	0.07
			Threshold 2	0.29	0.29		0.29	0.29
			Correlation	0.81			0.55	

# ACEcat\_smk.mx

```
#define nvar 1           !number of variables per twin
#define nvarx2 2        !number of variables per pair
#define nthresh 2       !number of thresholds=num of cat-1
#ngroups 4             !number of groups in script

G1: Parameters for the Genetic model
Calculation
Begin Matrices;
X Low nvar nvar FREE   !Additive genetic path coefficient
Y Low nvar nvar FREE   !Common environmental path coefficient
Z Low nvar nvar FREE   !Unique environmental path coefficient
End matrices;
Begin Algebra;
A=X*X' ;               !Additive genetic variance (path X squared)
C=Y*Y' ;               !Common Environm variance (path Y squared)
E=Z*Z' ;               !Unique Environm variance (path Z squared)
End Algebra;
start .6 X 1 1 Y 1 1 Z 1 1 !starting value for X, Y, Z
Interval @95 A 1 1 C 1 1 E 1 1!requests the 95%CI for h2, c2, e2
End
```

G2: Data and model for MZ pairs

Data NInput\_vars=3

Missing=.

Ordinal File=prac\_smk.ord

Labels

zyg ageon\_t1 ageon\_t2

SELECT IF zyg = 2

SELECT ageon\_t1 ageon\_t2 /

Matrices = group 1

T FULL nthresh nvarx2 FREE

L Lower nthresh nthresh

!Thresholds for twin 1 and twin 2

COV

!Predicted covariance matrix for MZs

( A + C + E | A + C  
A + C | A + C + E ) /

Thresholds L\*T /

!Threshold model

Bound 0.01 1 T 1 1 T 1 2

!Ensures +ve threshold increment

Bound 0.1 5 T 2 1 T 2 2

Start 0.1 T 1 1 T 1 2

!Starting values for the 1st thresholds

Start 0.2 T 1 1 T 1 2

!Starting values for increment

Option rs

End

G3: Data and model for DZ pairs

DATA NInput\_vars=4

Missing=.

Ordinal File=prac\_smk.ord

Labels

zyg ageon\_t1 ageon\_t2

SELECT IF zyg = 4

SELECT ageon\_t1 ageon\_t2 /

Matrices = group 1

T FULL nthresh nvarx2 FREE

!Thresholds for twin 1 and twin 2

L Lower nthresh nthresh

H FULL 1 1

!0.5

COVARIANCE

!Predicted covariance matrix for DZs

( A + C + E | H@A + C  
H@A + C | A + C + E ) /

Thresholds L\*T /

!Threshold model

Bound 0.1 1 T 1 1 T 1 2

!Ensures +ve threshold increment

Bound 0.1 5 T 2 1 T 2 2

Start 0.1 T 1 1 T 1 2

!Starting values for the 1st thresholds

Start 0.2 T 1 1 T 1 2

!Starting values for increment

Option rs

End

G4: CONSTRAIN VARIANCES OF OBSERVED VARIABLES TO 1

CONSTRAINT

Matrices = Group 1

I UNIT 1 1

CO A+C+E= I / **!constrains the total variance to equal 1**

Option func=1.E-10

End

## Constraint groups and degrees of freedom

As the total variance is constrained to unity, we can estimate one VC from the other two, giving us one less independent parameter:

$$A + C + E = 1 \quad \text{therefore} \quad E = 1 - A - C$$

So each constraint group adds a degree of freedom to the model.

# Exercise II

- Fit ACE model
  - What does the threshold model look like?
    - Change it to reflect the findings from exercise I
  - What are the VC estimates?

**Raw ORD File: smk\_prac.ord**  
**Script: ACEcat\_smk.mx**  
**Location:**  
**Faculty\Fruhling\Categorical\_Data**



# Results

Model	-2LL	df	$\chi^2$	df	P
Saturated	5128.185	3055			
ACE	5130.628	3061	2.443	6	0.88

### 3 Confidence intervals requested in group 1

Matrix	Element	Int.	Estimate	Lower	Upper	Lfail	Ufail
A	1	1	95.0	0.5254	0.3278	0.7391	0 0 0 0
C	1	1	95.0	0.2862	0.0846	0.4659	0 0 0 0
E	1	1	95.0	0.1884	0.1476	0.2376	6 1 0 1