Comorobidity Models

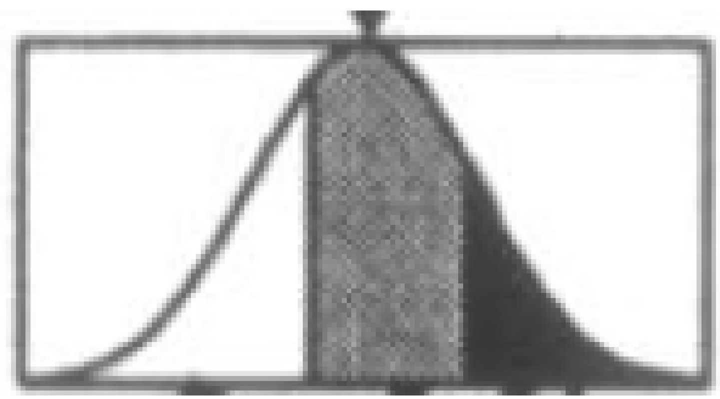
NIDA Advanced Genetic Epidemiology Workshop

Introduction

- Substance use and disorders diagnosis is highly comorbid with other psychiatric disorders, such as depression, schizophrenia.
- Questions: are the two disorders distinct or do they reflect an arbitrary division of a single syndrome?

Threshold model for liability

- Disease liability arises from the independent action of a large number of factors, each of small effect, which give rise to a normal distribution of liability. In the basic threshold model, individuals above an abrupt threshold have the disorder, whereas those below do not.



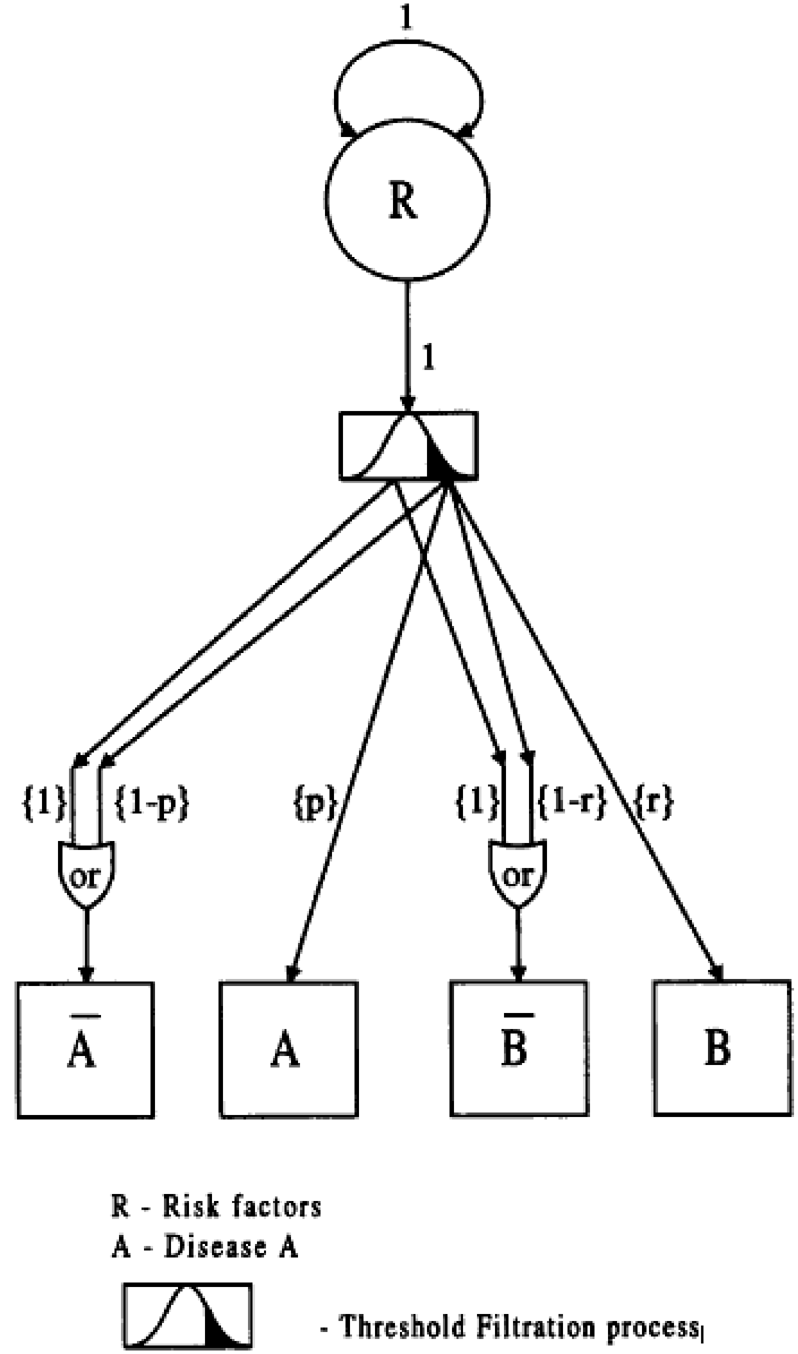
Model 1. Alternate Forms

$$P(\bar{A}, \bar{B}) = L + (1 - p)(1 - r)U$$

$$P(\bar{A}, B) = p(1 - r)U$$

$$P(A, \bar{B}) = (1 - p)rU$$

$$P(A, B) = prU ,$$



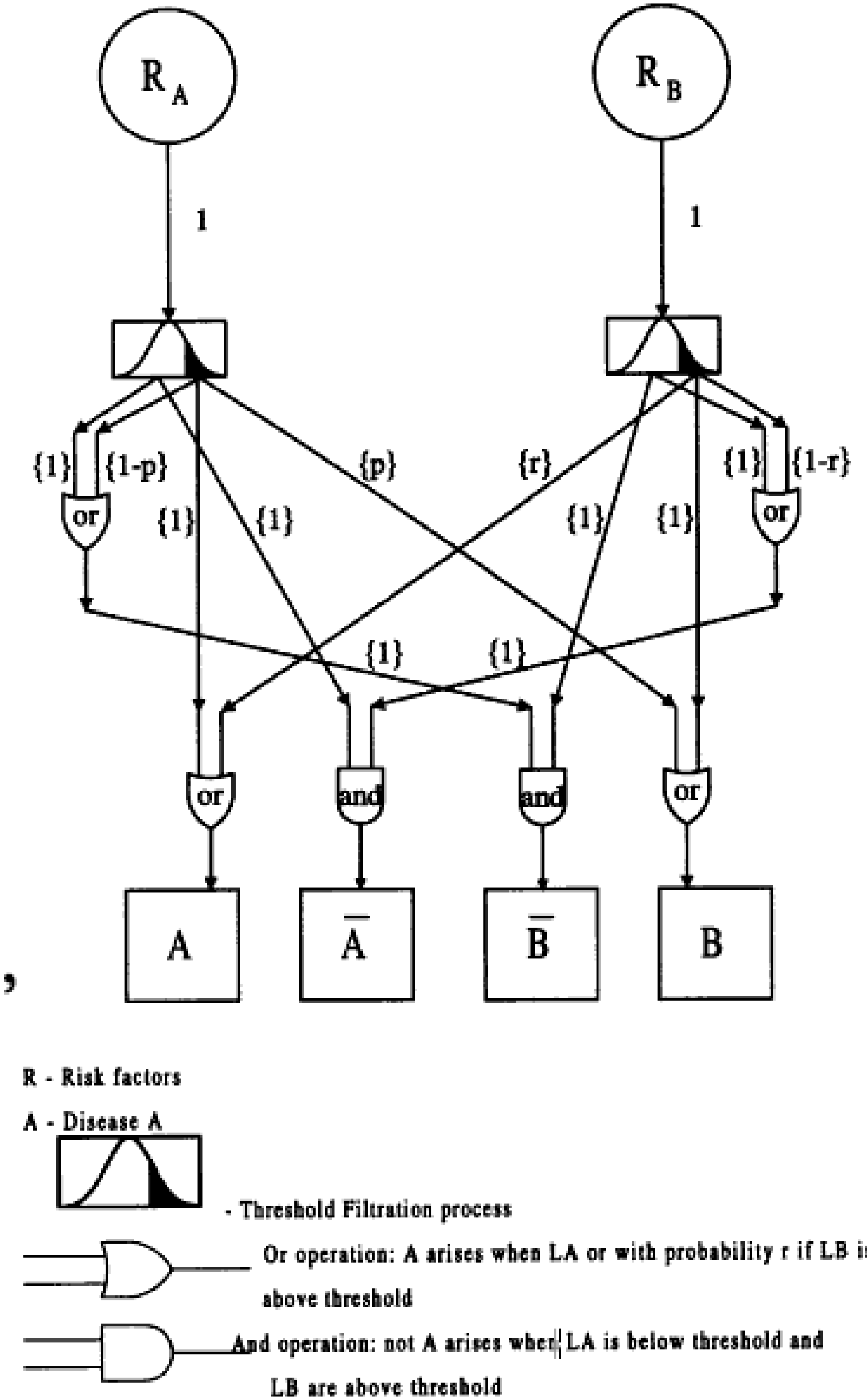
Model 2. Random Multiformity

$$P(\bar{A}, \bar{B}) = L_A \cdot L_B$$

$$P(\bar{A}, B) = (1 - r)L_A \cdot U_B$$

$$P(A, \bar{B}) = U_A \cdot (1 - p)L_B$$

$$P(A, B) = U_A \cdot (U_B + pL_B) + rL_A \cdot U_B \ ,$$



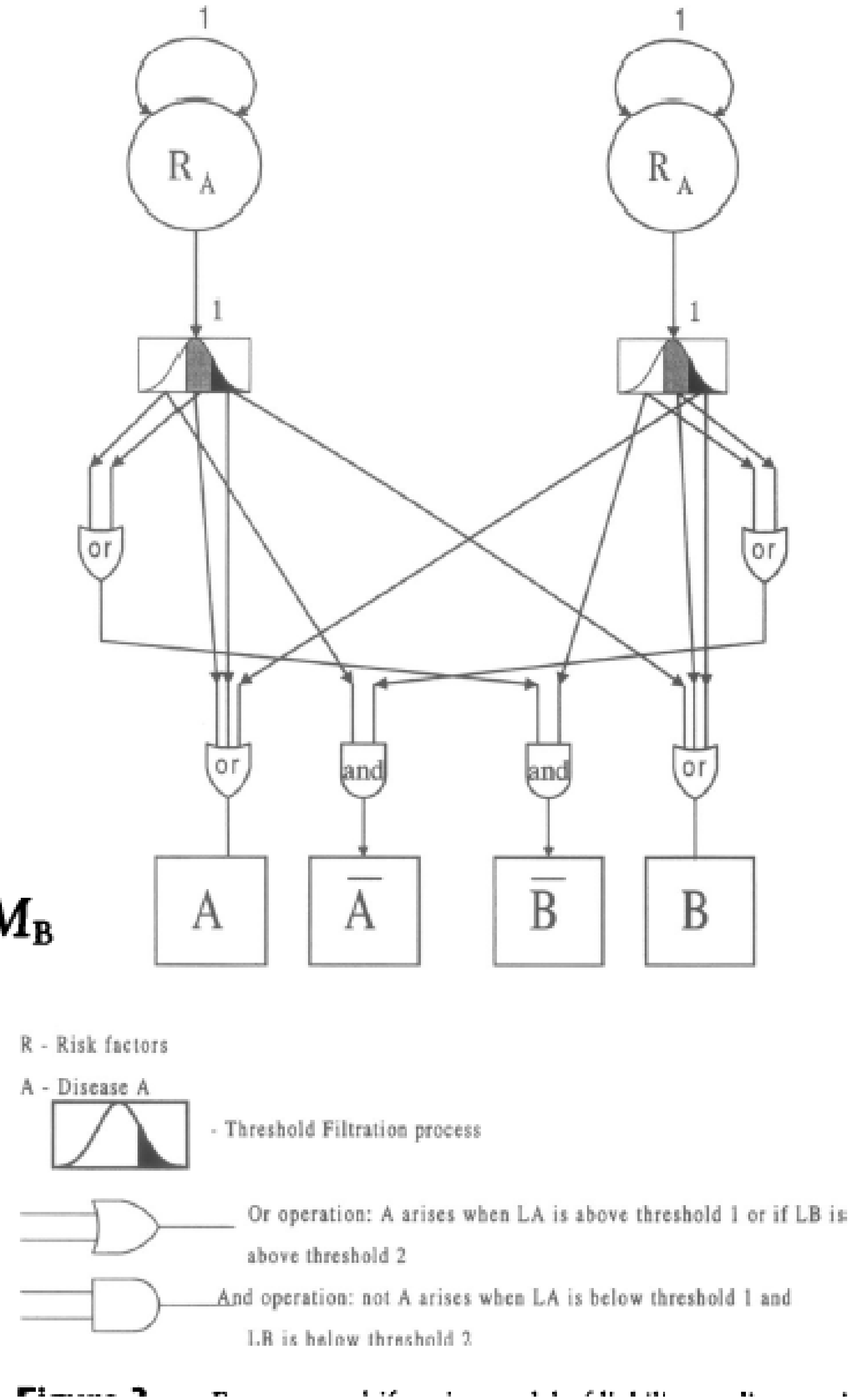
Model 3. Extreme Multiformity

$$P(\bar{A}, \bar{B}) = L_A \cdot L_B$$

$$P(\bar{A}, B) = L_A \cdot M_B$$

$$P(A, \bar{B}) = M_A \cdot L_B$$

$$P(A, B) = U_A + U_B - U_A \cdot U_B + M_A \cdot M_B$$



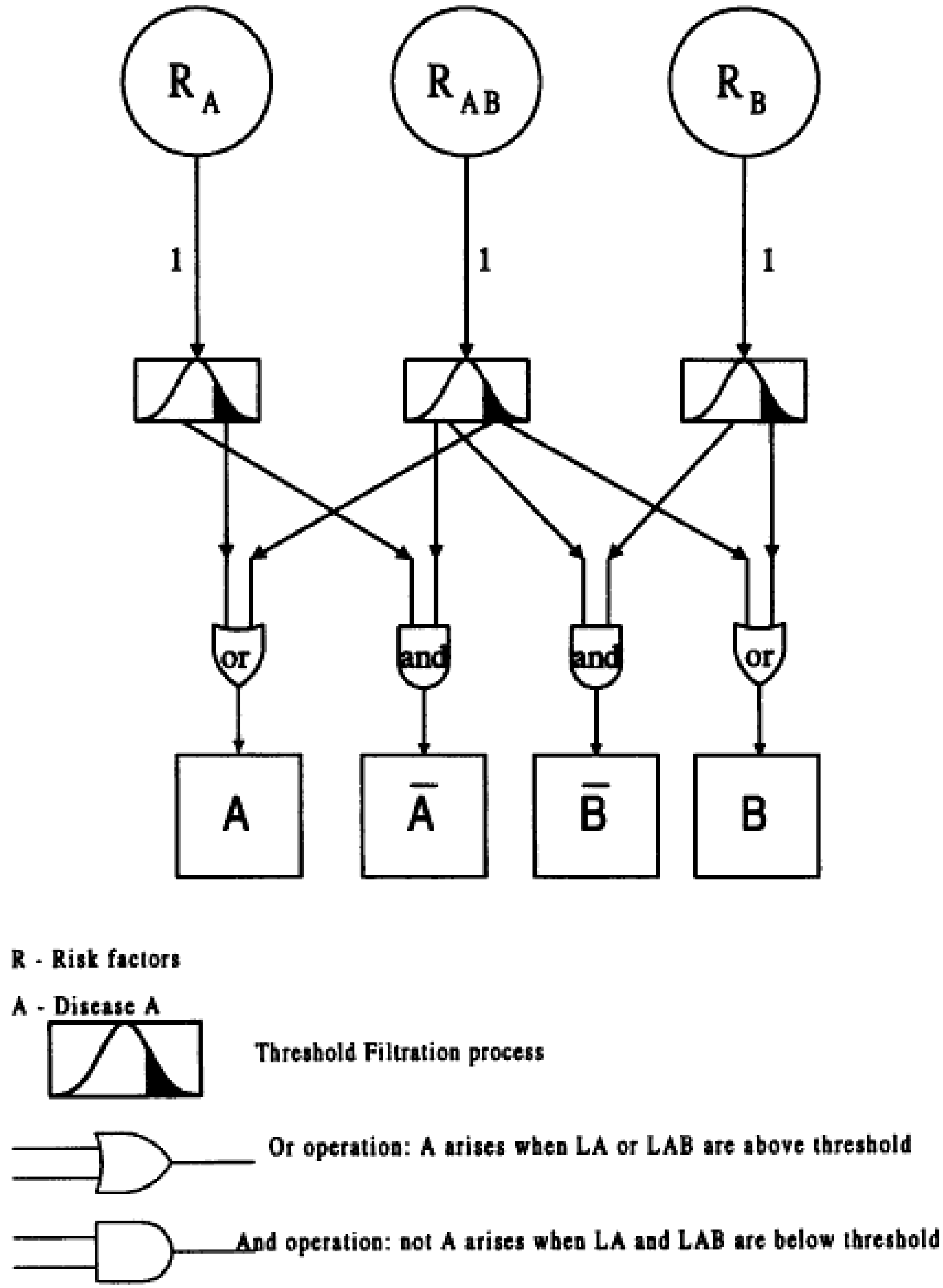
Model 4. Three independent

$$P(\bar{A}, \bar{B}) = L_A \cdot L_{AB} \cdot L_B$$

$$P(\bar{A}, B) = L_A \cdot L_{AB} \cdot U_B$$

$$P(A, \bar{B}) = U_A \cdot L_{AB} \cdot L_B$$

$$P(A, B) = U_A \cdot L_A B \cdot U_B + U_{AB}$$



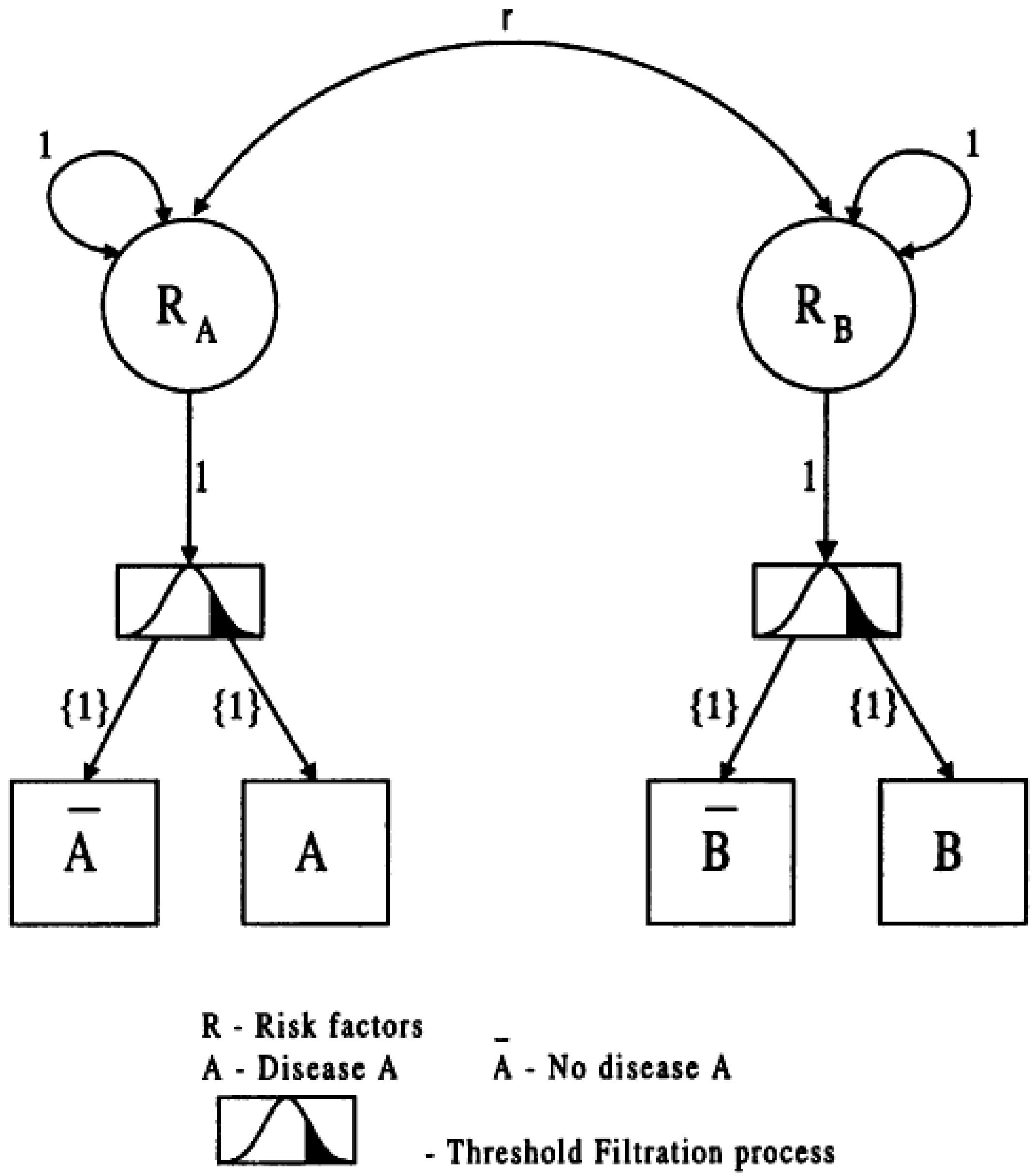
Model 4. Correlated Liability

$$P(\bar{A}, \bar{B}) = LL_{A,B}$$

$$P(\bar{A}, B) = LU_{A,B}$$

$$P(A, \bar{B}) = UL_{A,B}$$

$$P(A, B) = UU_{A,B}$$



Data Tabulation

Twin 1 \ Twin 2		No		Yes	
		No	Yes	No	Yes
No	No	----	---+	--+-	--++
	Yes	-+--	-+-+	-++-	-+++
Yes	No	+---	+--+	+-+-	+-++
	Yes	++--	++-+	+++-	++++

10 Flavors: Sum across Diagonal

Twin 2 / Twin 1		No		Yes	
		No	Yes	No	Yes
No	No	----	---+	--+-	--++
	Yes		-+-+	-++-	-+++
Yes	No			+-+-	+-++
	Yes				++++

---+
--+-
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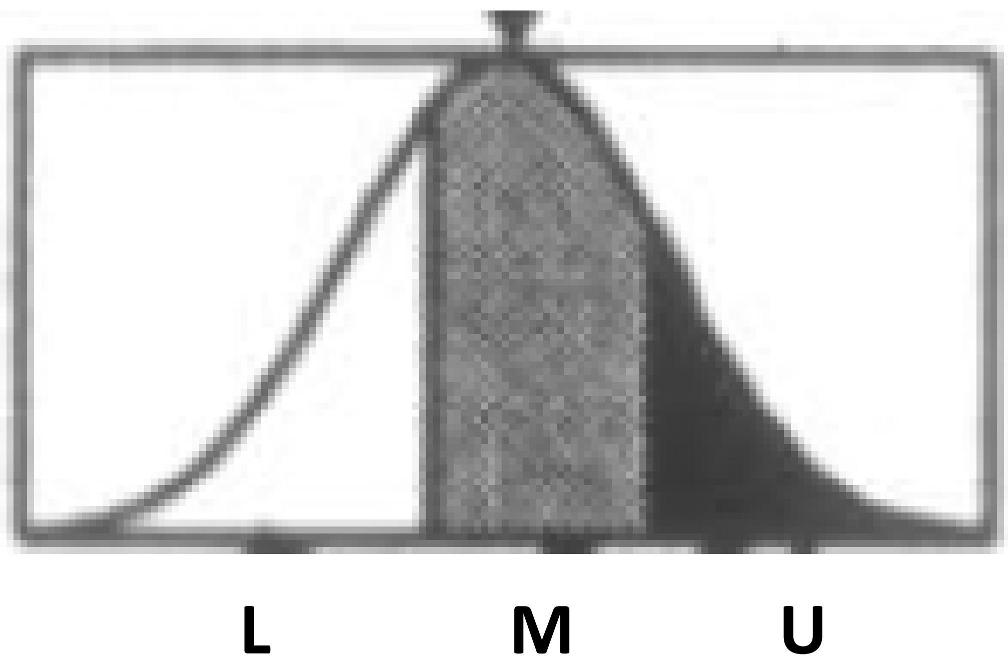
Observed Frequencies for Pairwise Diagnostic Data on MD and in MZ and DZ Female Twins

		Twin 1			
		No MD		MD	
Twin 2		No GAD	GAD	No GAD	GAD
		A. MZ Twins			
No MD	No GAD	282	25	54	29
No MD	GAD	19	3	3	9
MD	No GAD	31	10	8	18
MD	GAD	36	6	9	28
		B. DZ Twins			
No MD	No GAD	155	20	38	34
No MD	GAD	22	4	1	9
MD	No GAD	38	8	11	13
MD	GAD	42	6	21	18

	Twin 1	Twin2
LL_A	L	L
LM_A	L	M
LU_A	L	U
MM_A	M	M
MU_A	M	U
UU_A	U	U



Model 1. Alternate Forms

$$P(\bar{A}1, \bar{B}1, \bar{A}2, \bar{B}2) = LL + 2(1-p)(1-r)UL + (1-p)^2(1-r)^2UU$$

$$P(\bar{A}1, \bar{B}1, \bar{A}2, B2) = r(1-p)LU + (1-p)^2r(1-r)^2UU$$

$$P(\bar{A}1, \bar{B}1, A2, \bar{B}2) = p(1-r)LU + p(1-p)(1-r)^2UU$$

$$P(\bar{A}1, \bar{B}1, A2, B2) = prLU + p(1-p)r(1-r)UU$$

$$P(\bar{A}1, B1, \bar{A}2, B2) = (1-p)^2r^2UU$$

$$P(\bar{A}1, B1, A2, \bar{B}2) = p(1-p)r(1-r)UU$$

$$P(\bar{A}1, B1, A2, B2) = p(1-p)r^2UU$$

$$P(A1, \bar{B}1, A2, \bar{B}2) = p^2(1-r)^2UU$$

$$P(A1, \bar{B}1, A2, B2) = p^2r(1-r)UU$$

$$P(A1, B1, A2, B2) = p^2r^2UU\,.$$

Model fitting

$$F = \sum_{i=1}^{10} \frac{(O_i - E_i)^2}{E_i}$$

Fit Statistics Obtained for Various Models of Comorbidity Applied to Data on GAD and MD in Adult Female Twins

Model Number and Name	Fit Statistic			
	χ^2	df	p	AIC
1 (Chance)	412.54	12	.00	388.54
2 (Alternate forms)	23.74	13	.03	−2.26
3 (Random multiformity)	25.59	10	.04	5.59
4 (Random multiformity of MD)	26.19	11	.06	4.19
5 (Random multiformity of GAD)	40.89	11	.00	18.89
6 (Extreme multiformity)	16.51	10	.08	−3.49
7 (Extreme multiformity of MD)	21.76	11	.03	−.24
8 (Extreme multiformity of GAD)	37.02	11	.00	15.02
9 (Three independent disorders)	39.77	9	.00	21.77
10 (Correlated liabilities)	12.23	9	.20	−5.77
11 (MD causes GAD)	14.79	11	.19	−7.21
12 (GAD causes MD)	21.09	11	.03	−.91
13 (Reciprocal causation)	12.29	10	.27	−7.71