

This is a preprint of an article published in the British Journal of Psychiatry.

Fergusson DM, Horwood LJ, Boden JM. Structure of internalizing symptoms in early adulthood. *British Journal of Psychiatry*, 2006; 189: 540-546.

Structure of internalizing symptoms in early adulthood

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ABSTRACT

Background: Debate surrounds the underlying structure of internalizing disorders including major depression (MD), generalized anxiety disorder (GAD), phobias and panic disorders (PD).

Aims: To model the within-time and across-time relationships of internalizing symptoms incorporating effects from generalized internalizing and disorder-specific components of continuity.

Method: Data were gathered from a 25-year longitudinal study of a birth cohort of New Zealand children (n = 973). Outcome measures included DSM-IV symptom scores for MD, GAD, phobia and PD at age 18, 21 and 25 years.

Results: Structural equation modelling showed that, within times, a common underlying measure of generalized internalizing explained symptom score comorbidities. Across-time correlation of symptom scores was primarily accounted for by continuity over time in generalized internalizing. However, for MD and phobia there was also evidence of across-time continuity in the disorder-specific components of symptoms.

Conclusions: Internalizing symptoms can be partitioned into components reflecting both a generalized tendency to internalizing and disorder-specific components.

Declaration of Interest: None

There has been a large amount of research, debate and speculation about the classification of internalizing disorders including major depression (MD), generalized anxiety disorder (GAD), phobia and panic disorders (see for example (Kovacs & Devlin, 1998; Lilienfeld, 2003; Watson, 2005; Zahn-Waxler, Klimes-Dougan & Slattery, 2000). A central issue in these debates has concerned the extent to which internalizing disorders are reflections of a common underlying disorder of internalizing and the extent to which these disorders are distinct diagnostic entities (Brown, Chorpita & Barlow, 1998; Hartman, Hox, Mellenbergh, *et al*, 2001; Hettema, Prescott & Kendler, 2004; Hudson, Mangweth, Pope, *et al*, 2003; Kendler, 2004; Kendler, Neale, Kessler, *et al*, 1992; Khan, Jacobson, Gardner, *et al*, 2005; Krueger, 1999; Krueger, Caspi, Moffitt, *et al*, 1998; Schoevers, Deeg, van Tilburg, *et al*, 2005; Vollebergh, Iedema, Bijl, *et al*, 2001; Watson, 2005). Resolution of this issue is central to both the development of methods for classifying internalizing disorders and for understanding the aetiological processes that underlie these disorders (Brown, Chorpita & Barlow, 1998; Clark, 2005; Hettema, Prescott & Kendler, 2004; Hudson, Mangweth, Pope, *et al*, 2003; Kendler, Neale, Kessler, *et al*, 1992; Kovacs & Devlin, 1998; Krueger, 1999; Krueger, Caspi, Moffitt, *et al*, 1998; Lilienfeld, 2003).

In this paper we develop a structural equation model of the underlying structure of internalizing disorder symptoms and fit this model to data gathered on a birth cohort of nearly 1000 young people studied on three occasions over the period from 18 to 25 years. The general aims of this model were to examine the role of generalized and disorder-specific factors in the within-time comorbidity of disorder and the across-time continuity of disorders. Underlying this model is a general concern with estimating the fraction of variance and covariance between internalizing symptoms can be explained by a generalized tendency to internalizing and how much of this variance and covariance is disorder-specific.

BACKGROUND TO THE MODEL

Figure 1 shows a conceptual model of the within- and across-time structure of internalizing symptoms (MD, GAD, phobia, panic) assessed at three time periods (t1, t2, t3). The structure of the model can be thought of as comprising two linked components:

1. The within-time model that assumes that the observed symptom measures of MD, GAD, phobia and panic at each time t are linked by a common factor model in which the variance in the symptom scores reflects: a) variation due to a generalized internalizing factor (I_t); and b) variation specific to each disorder (U_{it}).
2. The across-time model that assumes that continuities between disorders can arise by two routes: a) continuity mediated via the continuity of the generalized internalizing factor across time; and b) disorder-specific continuity.

If it is assumed that all relationships within the model are linear and additive, then the model in figure 1 may be written as a structural equation model. The full specification of the model is given in the statistical section of Methods.

INSERT FIGURE 1 HERE

The major advantage of the conceptual model in figure 1 is that it resolves the lumpers/splitters debate by partitioning the variance of the symptom scores into components reflecting generalized internalizing and disorder-specific variance. Further, the across-time model makes it possible to examine the extent to which continuities in internalizing symptoms are mediated by the across-time stability of generalized internalizing or via disorder-specific pathways. Finally, the model has the advantage of being testable since the number of model parameters is smaller than the number of observed variances and covariances (see Methods for a discussion of the identification status of the model).

In the remainder of this paper we will fit the model in figure 1 to data gathered on DSM-IV internalizing symptoms gathered on a birth cohort of young adults studied at ages 18, 21 and 25. The aims of this analysis are: a) to determine the extent to which the model in figure 1 provides an adequate account of within and across-time relationships between internalizing disorder symptoms and b) to examine the implications of the model for diagnostic classification and the understanding of the origins of internalizing disorders.

METHOD

PARTICIPANTS

The data were gathered during the course of the Christchurch Health and Development Study (CHDS). In this study a birth cohort of 1265 children (635 males, 630 females) born in the Christchurch (New Zealand) urban region in mid-1977 has been studied at birth, 4 months, 1 year and annually to age 16 years, and again at ages 18, 21 and 25 years (Fergusson & Horwood, 2001; Fergusson, Horwood, Shannon, *et al*, 1989). The present analyses are based on the sample of 953 study participants who were interviewed on measures of internalizing disorders at ages 18, 21 and 25 years. This sample represented 75% of the initial cohort of 1265 participants enrolled in the study. All study information was collected on the basis of signed and informed consent from study participants.

INTERNALIZING SYMPTOMS

At ages 18, 21 and 25 years study participants were interviewed on a structured mental health interview designed to assess aspects of mental health and psychosocial adjustment since the previous assessment. All interviews were conducted in private by trained lay interviewers at a location convenient to the respondent. As part of the mental health assessment at each age, components of the Composite International Diagnostic Interview (CIDI) (World Health

Organization, 1993) were used to assess DSM-IV symptom criteria for a range of internalizing disorders including: MD, GAD, social phobia, specific phobia, and panic disorder with or without agoraphobia. Using these data summary measures of the extent of internalizing disorder symptomatology were constructed for each of the periods 16-18 years, 18-21 years and 21-25 years in the following ways.

1. Major Depression: At each interview participants were questioned about major depressive symptoms occurring in the past month, the past 12 months and the period back to the time of the previous assessment. Participants who at any time reported a depressive episode involving either of the two core symptom criteria for major depression (feeling sad miserable or depressed; loss of interest in daily activities) were further questioned about the occurrence of other DSM-IV symptom criteria. For the purposes of the present analysis a depressive symptoms score was constructed for each assessment period based on a count of the number of DSM-IV MD symptom criteria reported at any time during the assessment period.
2. Generalized Anxiety Disorder: At each interview participants were questioned about the occurrence of episodes of feeling tense, anxious or worried most of the time since the previous assessment. Young people who reported an episode lasting at least one month or longer were further questioned about the duration and source of the anxiety and associated DSM-IV symptomatology. For the purposes of the present analysis a GAD symptom score was constructed for each assessment period based on a count of the number of anxiety symptoms reported from the following list of DSM-IV symptom criteria: feeling restless, keyed up or on edge; getting tired very easily; having difficulty concentrating; feeling irritable; muscles feeling tense, sore or aching; having trouble getting asleep or staying asleep.
3. Phobia: Participants were questioned about DSM-IV symptom criteria for social and specific phobia including the nature of the fear, the level of distress experienced, avoidant behaviours, the extent of impairment of functioning and the extent of anxiety symptomatology experienced upon exposure to the source. For the purposes of the present analysis a phobia symptoms score

was computed for each interview period based on a count of the number of anxiety symptoms that the young person reported experiencing when exposed to any social or specific phobia stimulus. These symptoms included: feeling nervous and panicky; sweating; heart beating faster; shortness of breath; blushing or shaking; feeling like vomiting; concern that they might do something embarrassing.

4. Panic: At each interview participants were questioned about panic attacks occurring since the previous assessment and CIDI items were used to assess relevant DSM-IV symptom criteria. As part of this questioning, participants were asked to describe their most serious panic attack occurring during the interview period and any associated symptomatology. For the purposes of the present analysis a panic symptoms score was created for each interview period based on a count of the number of panic attack symptoms reported for the most severe attack out of the list of 13 DSM-IV symptom criteria. In view of the low base rate of panic no attempt was made to distinguish between panic attacks occurring in the presence or absence of agoraphobia.

STATISTICAL ANALYSIS

The above measures of internalizing comprising four symptom scores (MD, GAD, phobia, panic) assessed at three time periods formed the input data for fitting the model depicted in figure 1. Let Y_{it} represent the symptom score for the i -th diagnostic domain ($i = 1, 2, 3, 4$) at the t -th time period ($t = 1, 2, 3$), I_t represent the measure of generalized internalizing at each time t and U_{it} the disorder-specific component of Y_{it} . Then, subject to the assumption that the associations between variables are linear and additive, this model may be represented as a structural equation model defined by the following system of equations.

Within-time model:

$$Y_{it} = \lambda_{it} I_t + U_{it} \quad i = 1, 2, 3, 4 \quad t = 1, 2, 3$$

Across-time model:

$$I_t = \gamma_t I_{t-1} + E_t \quad t = 2, 3$$

$$U_{it} = \lambda_{it} U_{it-1} + W_{it} \quad i = 1, 2, 3, 4 \quad t = 2, 3$$

In these equations the coefficients λ_{it} represent the factor loadings of the observed symptom scores (Y_{it}) on the underlying measures of generalized internalizing (I_t). If all variables in the model are standardized the squares of these coefficients represent the proportion of variance in the observed symptom scores that is accounted for by generalized internalizing. The across-time continuities in generalized internalizing (I_t) and disorder-specific components (U_{it}) are assumed to be related by an auto-regressive model with coefficients γ_t and λ_{it} respectively. The terms E_t and W_{it} represent disturbance terms in the across-time components of the model. These disturbance terms are assumed to be mutually uncorrelated. In addition, the model assumes that both the disorder-specific components U_{it} and the disturbances W_{it} are uncorrelated with the measures of generalized internalizing I_t .

The above model may be fitted to the correlation matrix of the 12 observed symptom scores (4 disorder symptom scores at 3 times). A necessary condition for the model to be identifiable (estimable) is that the number of model parameters to be estimated is less than or equal to the number of non-redundant elements (k) of the observed correlation matrix ($k = 78$). The model specification for figure 1 has a total of 34 parameters to be estimated (12 factor loadings λ_{it} , 8 parameters λ_{it} , 2 parameters γ_t , and 12 variances for the terms U_{it} and W_{it}). The model is identified with 44 degrees of freedom. Further because the number of model parameters is substantially less than the number of non-redundant correlation elements, the model is falsifiable to the extent that an inadequate model may be rejected on the basis of a poor fit to the observed data.

In the present analysis models were fitted to the matrix of polychoric correlations between the observed symptom measures. Model fitting was conducted using LISREL 8 (Joreskog & Sorbom, 1993a) and methods of weighted least squares estimation. These methods are more appropriate for the situation in which data are non-normally distributed (Joreskog & Sorbom, 1993a) and were used in the present instance because the observed symptom report data were highly skewed. Assessment of model fit was based on evaluation of a number of fit indices including the

chi squared goodness of fit index, the root mean squared error of approximation (RMSEA), the root mean squared residual correlation (RMSR), the adjusted goodness-of-fit index (AGFI), and the comparative fit index (CFI). A well-fitting model should have an RMSEA of less than .05, an RMSR close to zero, and AGFI, and CFI indices close to 1 (Joreskog & Sorbom, 1993b). Finally, the model was extended to include gender, and tests of gender heterogeneity were conducted using the multiple indicators, multiple causes (MIMIC) modelling approach described by Muthen. (Muthen, 1989).

RESULTS

CORRELATIONS

Table 1 shows the matrix of polychoric correlations between the measures of MD, GAD, phobia and panic symptom scores assessed at ages 16-18, 18-21 and 21-25 years. This Table shows the presence of significant correlations between measures both within and across time periods.

IN SERT TABLE 1 HERE

MODEL FITTING

The conceptual model in figure 1 showed a generally good fit to the data in terms of measures of goodness-of-fit (RMSEA = .032, p-value for test of close fit (RMSEA < .05) = .99; RMSR = .065; AGFI = .98; CFI = .98). However, the model chi-square statistic proved to be significant ($\chi^2 = 85.5$; $df = 44$; $p = .0002$). Examination of modification indices and model residuals suggested the model fit could be significantly improved by two changes to the original model specification: (i) For MD and phobia an additional disorder-specific pathway from time 1 (age 18) to time 3 (age 25) was

included in the model; (ii) The disorder-specific components of MD and GAD were permitted to be correlated within measurement periods.

These changes in model structure led to a significant improvement in model fit ($\Delta\chi^2 = 24.0$, $df = 5$, $p < .001$) and produced an adequately fitting model on the basis of the fit indices (RMSEA = .025, p-value for test of close fit (RMSEA < .05) = 1.00; RMSR = .056; AGFI = .98; CFI = .99). The final fitted model is shown in figure 2. The figure gives the standardized model parameters. For ease of presentation non-significant ($p > .05$) pathways and some disturbance terms have been omitted from the model. Examination of the figure shows:

INSERT FIGURE 2 HERE

MODEL INTERPRETATION

1. The within-time structure: The fitted model shows that each of the measures (MD, GAD, phobia and panic) had strong and statistically significant loadings on the generalized internalizing factor. These loadings ranged from .64 to .89 with a median value of .66. This aspect of the model makes it possible to decompose the variance of each test at each time into two uncorrelated components: a) the test variance that was in common with the generalized internalizing measure; b) the test variance specific to the measure. These variance decompositions are shown in Table 2. This Table shows that the generalized internalizing factor explained in the region of: 43-45% of the variance in MD symptoms; 46-49% of the variance in GAD symptoms; 38-40% of the variance in phobia symptoms; and 67-72% of the variance in panic symptoms. These results suggest that the generalized internalizing factor explained from just under half to nearly three quarters of the observed symptom score variance, with the remaining variance including error variance being specific to the test. Further, aside from the small correlation between the residuals for MD and GAD, all of the within-time comorbidity of the observed symptom scores was explained by generalized internalizing.

INSERT TABLE 2 HERE

2. The across-time structure: The fitted model shows that there were two general routes leading to the across-time continuity of symptom scores. First, this continuity was mediated by the linkages between each test and the generalized internalizing factor. Second, there was homotypic continuity independently of the mediating effect of generalized internalizing. These features of the model make it possible to decompose the across-time correlations of tests into two additive components: a) the component mediated via generalized internalizing; b) the component independent of generalized internalizing. These decompositions are given in Table 3.
3. The table shows that all of the across-time continuity of GAD and Panic symptoms was mediated by generalized internalizing. However, for MD and phobia there was evidence of further pathways in which the presence of symptoms at one time influenced the same type of symptoms at a later time independently of the effects of generalized internalizing. The results show that for MD symptoms in the region of 63-69% of the across-time correlations was mediated via generalized internalizing and the remainder was specific to depression. For phobia symptoms, between 55-58% of the across-time correlations was mediated via generalized internalizing and the remainder was specific to phobia.

INSERT TABLE 3 HERE

SUPPLEMENTARY ANALYSIS

3. Gender differences. To examine the extent to which the core model structure varied with gender, the model fitted in figure 2 was extended to include gender and the methods described by Muthen (Muthen, 1989) used to test for gender heterogeneity. This analysis showed that gender was significantly correlated with the measures of generalized internalizing ($r = .28$ to

.47, $p < .001$), reflecting a significant tendency for females to exhibit higher general levels of internalizing behavior. However, there was no evidence to suggest that other aspects of model structure, including the factor loadings for the internalizing symptom scores and the continuities of either the generalized internalizing or the specific disorder components, varied with gender.

DISCUSSION

In this paper we have used data gathered over the course of a longitudinal study to examine the within- and across-time structure of DSM-IV symptom measures of internalizing disorders including major depression, generalized anxiety disorder, phobias and panic disorders. The best fitting structural model proved to be a hybrid of two traditions that have dominated the description of internalizing symptoms. First, the results support the view that the current DSM disorder classifications represent unique and to some extent non-overlapping domains of internalizing behaviors. At the same time the model also suggests that the within-time comorbidity of these domains of disorder is explained by a common generalized internalizing factor. Thus there is evidence for both the lumpers and splitters positions on the classification of internalizing disorders, with some fraction of the variance in symptom scores reflecting a generalized dimension of internalizing whereas the remaining variance is disorder-specific. These conclusions are generally consistent with the results of previous models of symptoms data that have produced evidence for both lumpers and splitters positions (Krueger, 1999; Krueger, 2002; Mineka, Watson & Clark, 1998; Watson, 2005).

On occasions the diagnostic categories reported in nosologies such as DSM-IV are treated as though they represent homogenous disorders having a common set of aetiological factors. The present analysis suggests that such an interpretation is implausible, in that the origins of these disorders is likely to be complex and heterogeneous, reflecting factors that are common to all internalizing and factors that are specific to a given disorder. The model estimates suggest that in

the region of half to three quarters of the variance in disorder symptom scores reflects a generalized internalizing factor with the remaining variance being specific to the specific disorders.

It has been well documented that internalizing disorders tend to recur and there is evidence of both homotypic continuity in which the same disorders show recurrence over time, and heterotypic continuity in which the onset of one disorder leads to an increased risk of the later onset of other internalizing disorders (Angold, Costello & Erkanli, 1999; Keller, Lavori, Mueller, *et al*, 1992; Keller, Lavori, Wunder, *et al*, 1992; Lilienfeld, 2003; McGee, Feehan, Williams, *et al*, 1992). An understanding of the development of internalizing disorders thus requires models which take into account both homotypic and heterotypic continuity. The model developed in this paper achieves this by permitting continuity of disorder by two routes. First, it is assumed that continuity of disorder may arise via the continuity of the generalized internalizing factor across time. Second, the model permits specific homotypic continuity of disorders. The fitted model leads to two major conclusions about the nature of across-time continuity in internalizing disorders. First, much of the across-time continuity in internalizing disorders reflects the strong across-time continuity of the internalizing factors. This result suggests that much of the homotypic and all of the heterotypic continuity in internalizing disorders arises because individuals predisposed to high levels of internalizing show the recurrence of the same disorders and the onset of new disorders.

At the same time the results make it clear that not all of the across-time continuity in internalizing disorders is mediated via generalized internalizing, and there is evidence of disorder-specific homotypic continuity with this being most marked for MD and phobias. In this respect the findings for across-time continuity mirror the findings for within-time comorbidity and suggest the presence of both a generalized internalizing component and disorder-specific components.

In turn these findings raise speculations about the interpretation of the generalised internalizing factors postulated in this analysis. This factor can be interpreted in at least three ways. First it may be suggested that this factor represents variation in individual predisposition to internalizing disorders. Under this interpretation, the generalised internalizing factor has a similar

interpretation to the personality trait of neuroticism (Eysenck, 1990). As a number of authors have pointed out, the trait of neuroticism may largely or wholly reflect individual variation in stable levels of internalizing symptoms (Duncan-Jones, Fergusson, Ormel, *et al*, 1990; Ormel, Rosmalen & Farmer, 2004). Second, it is possible that the internalizing factor does not represent a dimension of personality or disorder but rather is a latent variable that summarises the net effects of non-observed genetic and environmental factors on individual tendencies to internalizing symptoms. Finally, the internalizing factor could be conceptualised as a underlying dimension reflecting the extent of generalised internalizing disorder. This conceptualisation would support the view that there may be value in extending current systems of diagnostic classification to include a category of generalised internalizing disorder (GID). At the present time, there is no evidence to determine which of these interpretations is the more correct. Nonetheless, what the analysis does make clear is that there is considerable overlap, correlation and comorbidity between internalizing disorders with this overlap adequately represented by a single, general and highly stable latent dimension.

There are a number of important caveats that need to be placed on these results. First and foremost the findings describe the within- and across-time structure of internalizing disorders in a specific cohort, studied at a specific life stage using a specific set of measures. The extent to which the findings generalize beyond this context remains to be explored. A second potential limitation of the analysis is that we have assumed that the current DSM-IV groupings of internalizing symptoms into MD, GAD, phobias, and panic disorders provides a valid account of symptom variation. Further, to secure sufficient variation for analysis we have combined some disorders (notably phobias). These coding and classification rules may influence the results and conclusions drawn.

Despite these limitations the model developed in this paper has the major advantage that it provides a resolution to the long standing lumpers/splitter debate by showing that variation in internalizing symptoms can be partitioned into generalized and disorder-specific components with this dissection being evident in both within-time analyses of comorbidity and across-time analyses of continuity.

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Acknowledgements: This research was funded by grants from the Health Research Council of New Zealand, the National Child Health Research Foundation, the Canterbury Medical Research Foundation and the New Zealand Lottery Grants Board.

Contributions: DMF and LJH conceived of and designed the study, and DMF, LJH, and JMB analysed and interpreted data. DMF, LJH, and JMB drafted the article and revised the intellectual content. DMF, LJH, and JMB have all approved the submission of this version of the manuscript.

Table 1. Matrix of Polychoric Correlations Between MD, GAD, Phobia and Panic Symptom Scores (18, 21 and 25 Years).

Measure	Y11	Y21	Y31	Y41	Y12	Y22	Y32	Y42	Y13	Y23	Y33	Y43
<u>18 years</u>												
MD (Y11)	1.00											
GAD (Y21)	.56	1.00										
Phobia (Y31)	.45	.45	1.00									
Panic (Y41)	.55	.58	.57	1.00								
<u>21 Years</u>												
MD (Y12)	.51	.29	.30	.36	1.00							
GAD (Y22)	.41	.41	.28	.47	.51	1.00						
Phobia (Y32)	.33	.26	.51	.36	.35	.31	1.00					
Panic (Y42)	.38	.38	.37	.49	.49	.60	.60	1.00				
<u>25 Years</u>												
MD (Y13)	.38	.19	.21	.32	.48	.29	.27	.41	1.00			
GAD (Y23)	.28	.20	.18	.38	.39	.30	.22	.40	.57	1.00		
Phobia (Y33)	.28	.18	.42	.34	.27	.22	.56	.40	.37	.32	1.00	
Panic (Y43)	.17	.15	.21	.26	.34	.21	.36	.48	.52	.53	.44	1.00

Table 2. Percentage of Within Time Variance in Disorder Symptom Scores Due to Generalized Internalizing.

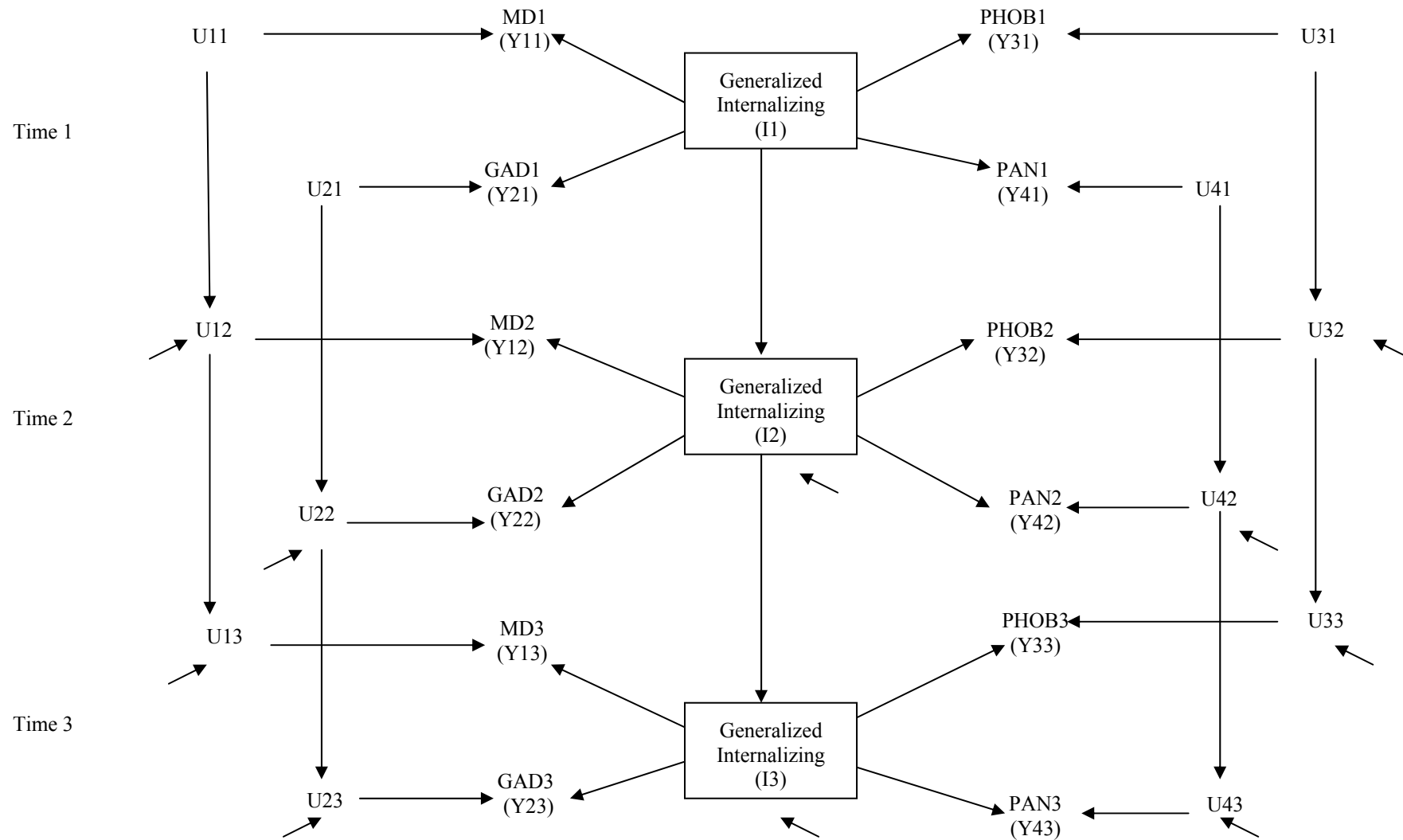
Symptom Measure	% of Variance Due to Internalizing		
	18 Years	21 Years	25 Years
MD	44.5	41.3	43.6
GAD	43.4	41.7	50.4
Phobia	39.3	41.6	36.8
Panic	75.0	78.3	61.8

Table 3. Decomposition of Across Time Correlations of Disorder Symptom Scores.

Correlation	Estimated Total Correlation From Fitted Model	Component Due to Continuity in Internalizing	Component Due to Disorder Specific Continuity
MD 18 → 21	.51	.31	.20
MD 21 → 25	.48	.33	.15
MD 18 → 25	.38	.25	.13
GAD 18 → 21	.39	.39	- *
GAD 21 → 25	.35	.35	- *
GAD 18 → 25	.26	.26	- *
Phobia 18 → 21	.50	.29	.21
Phobia 21 → 25	.54	.31	.23
Phobia 18 → 25	.39	.22	.17
Panic 18 → 21	.45	.45	- *
Panic 21 → 25	.52	.52	- *
Panic 18 → 25	.39	.39	- *

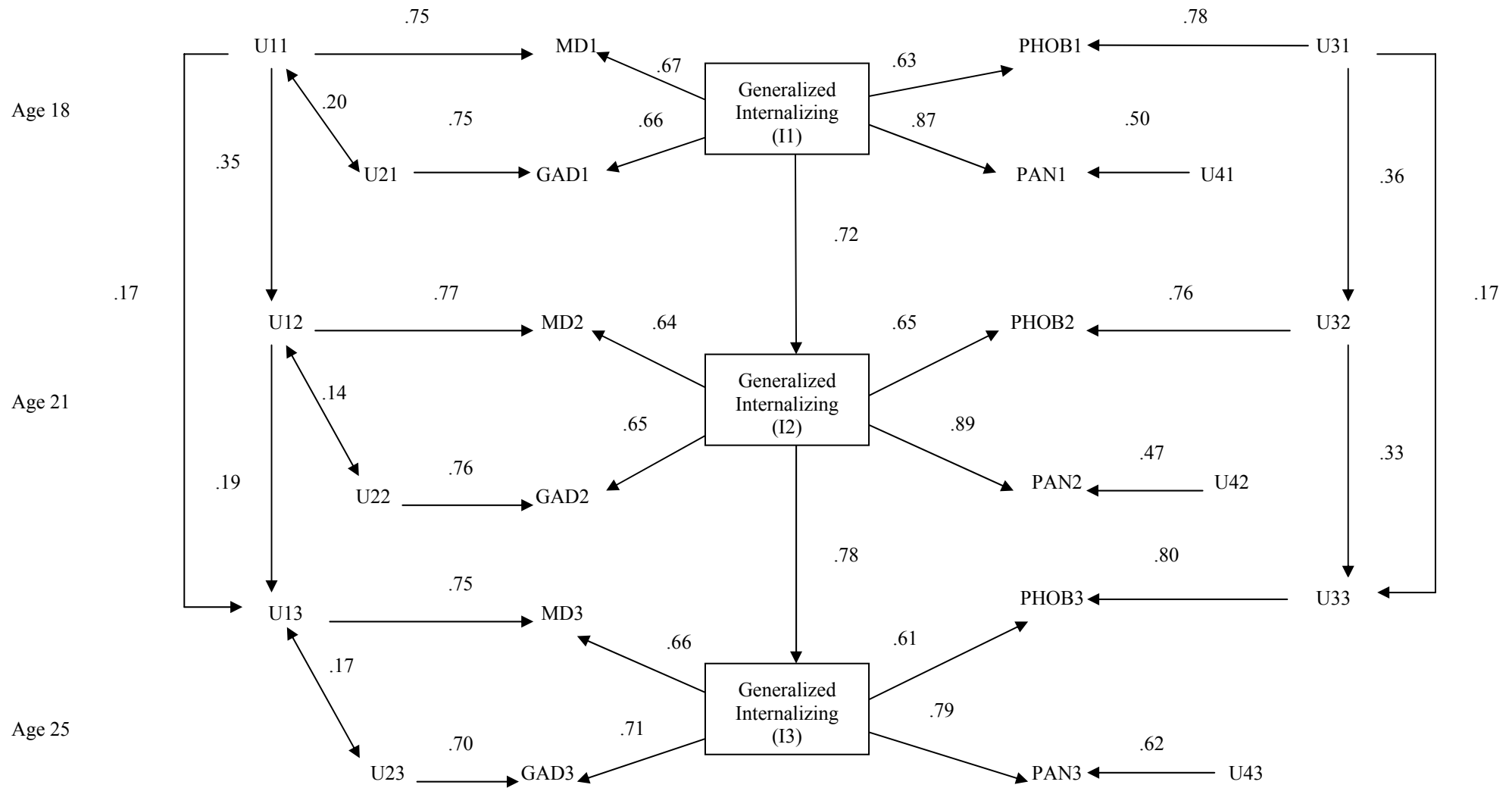
* Disorder specific pathway not significantly different from zero.

Figure 1. Hypothetical Model of Within Time and Across Time Structure of Internalizing Symptoms at Three Times.



Key: MD_t = Major depression symptom score at time t ; GAD_t = Generalised anxiety symptom score at time t ; $PHOBT$ = Phobia symptom score at time t ; PAN_t = Panic symptom score at time t ($t = 1, 2, 3$)

Figure 2. Fitted Model of Internalizing Symptoms at Ages 18, 21, and 25 Years.



Key: MD_t = Major depression symptom score at time t; GAD_t = Generalised anxiety symptom score at time t; PHOB_t = Phobia symptom score at time t; PAN_t = Panic symptom score at time t (t = 1, 2, 3)