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# GAD and MD: Common and reciprocal causes

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## Introduction

In their presentation on the correlation/overlap between major depression (MD) and generalised anxiety disorder (GAD), Kessler et al (2007) produce evidence to suggest a possible reciprocal relationship between MD and GAD . In this relationship prior MD was prognostic of later GAD and prior GAD prognostic of later MD.

While this study produces evidence consistent with the view that MD and GD may be causally related disorders, the analysis produced by Kessler it al does not fully distinguish between two processes that may lead MD and GAD to be related. First, MD and GAD may be related as a result of common causal processes that lead these conditions to co-occur. Second, there may be causal processes in which: a) the presence of MD leads to increased risks of GAD; or b) the presence of GAD leads to increased risks of MD.

This paper uses data gathered over the course of a longitudinal study of a birth cohort of New Zealand young adults to fit structural equation models that distinguish between the effects of common causes and cross lagged or reciprocal relationships between MD and GAD. This paper contributes to the debate on whether MD and GAD are separate disorders or the same disorder by examining the extent to which there may be causal relationships between these conditions over and above the effects of common causes.

## Methods

The data for this analysis come from the Christchurch Health and Development Study (CHDS). The CHDS is a longitudinal study of a birth cohort of 1,265 children born in the Christchurch (New Zealand) urban region during mid 1977. This cohort has been studied at regular periods to the age of 25. The data described in this report involve a cohort of 953 individuals studied at ages 18, 21, 25 using measures of MD and GAD.

1. The assessment of MD. 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. The assessment of GAD. 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.

Greater detail on the study and measurement of these disorders is given in Fergusson et al (2006).

**Results**

Table 1 shows the matrix of polychoric correlations between measures of MD and GAD at ages 18, 21, and 25. Inspection of this Table leads to three general conclusions.

First, there is a general tendency for all measures at all times to be inter-correlated. This evidence of pervasive correlation across diagnostic categories and time hints at the presence of common causal origins of MD and GAD.

Second, within time periods there are substantial correlations between GAD and MD reflecting the comorbidity of these conditions.

Third, there is evidence that the presence of GAD and MD at one time is predictive of GAD or MD at another time suggesting the presence of across time stability.

These observations suggest that models of GAD and MD need to take account of three causal structures: 1) The effects of common causes on GAD, MD; 2) Potentially reciprocal effects of MD and GAD; 3) the stability of disorder across time.

INSERT TABLE 1 ABOUT HERE

***Two Models of the Structure of MD and GAD Across Time***

Figures 1 and 2 present two structural equation models aimed at examining the role of common causes, reciprocal effects, and stability in measures of GAD and MD measured at three times (18, 21, 25 years). The models assume that:

1. The repeated measures of MD (MDt; t = 18, 21, 25) reflect a common underlying causal factor C1. Similarly the repeated measures of GAD (GADt; t = 18, 21, 25) reflect common underlying causal factor C2. Technically the factors C1, C2 are fixed effects which describe the fixed effects of common genes and environment on GADt and MDt.

2. The models then describe the structure of the residual terms Ut, Wt using different causal structures. Model 1 is a simultaneous reciprocal cause model in which, after correction for the correlation between C1, C2: MD is causally related to GAD by the parameter B1 and GAD is causally related to MD by the parameter B2. In addition early MD is related to later MD and early GAD to later GAD.

Model 2 is a cross lagged model that assumes that after correction for the correlation between C1 and C2, MD at time t is related to GAD at time t+1 by the parameter B1 and GAD at time t is related to MD at time t+1 by the parameter B2. This model provides an alternative to Model 1 by assuming a cross-lagged rather than simultaneous structure.

In terms of the issues raised by Kessler et al (2007) the critical issues focus on the values of B1, B2. Specifically, if there is a causal structure between MD and GAD after correction for common fixed causes it is necessary for at least one of the parameters to be non zero. Further, the size of these parameters may provide some guidance about the direction of any reciprocal effects.

***Model Results***

The models in Figures 1 and 2 were fitted to the data in Table 1 using weighted least squares. The results for each model are summarised in Table 2 which reports estimated of the model parameters and standard errors. In addition, the goodness of fit of each model is summarised by a series of indices. These results lead to the following conclusions:

1. **Model fit:** For both models the fit proved to be excellent, suggesting that the data in Table 1 were consistent with the proposed models. In terms of non nested measures of fit AIC, BIC the fit of either model was very similar, with the result that the models cannot be discriminated on the basis of goodness of fit.

2. **The role of common causes:** Both analyses show that the fixed effect factors C1, C2 were perfectly correlated. This result implies that the common fixed causes (genes, environment) were the same for both conditions.

3. **Reciprocal effects:** The model of reciprocal causes, Figure 1, suggests that while MD was related to GAD ($B = .88$; $p<.05$), GAD was not related to MD ($B = .013$; $p>.50$). The cross-lagged model (Figure 2) leads to a similar finding with lagged MD predicting GAD ($B = .23$; $p<.01$) but lagged GAD not being a predictor of MD ($B = .05$; $p>.50$). Both models lead to the consistent conclusion that if causal relationships exist between MD and GAD (after correction for common factors) these relationships involve a uni-causal association in which MD leads to GAD but GAD does not lead to MD.

4. **Stability:** Both models suggest some across time stability in MD and GAD over and above the effects of common causes.

INSERT TABLE 2 ABOUT HERE

**Discussion**

The analysis lead to two major conclusions about the origins of the correlation and comorbidity between MD and GAD.

First, in confirmation of a large amount of previous research there is evidence to suggest that GAD and MD are influenced by common causal factors that account for much of the correlation and comorbidity between these conditions. Second, in confirmation of the suggestions put forward by Kessler et al there is also evidence of additional causal pathways over and above the common causal factors. The results of this analysis lead to the conclusion that after common factors are taken into account changing depressive symptoms may lead to changes in GAD symptoms but changes in GAD symptoms do not lead to changes in MD symptoms. These results are only partially consistent with the conclusion draw by Kessler et al (2007) who suggest a bidirectional relationship. Nonetheless both studies are in agreement over the common point that there appear to be structural relationships between MD and GAD over and above the effects of common causes.

It must be stressed that the work in this paper is both exploratory and preliminary and is subject to a number of important caveats.

First, it is important to recognise that the model focuses on symptoms of GAD and MD rather than upon diagnostic measures. Findings for symptom level data may not translate readily to diagnostic classifications. Second, the process of model fitting raises some complex technical issues. In particular, to solve the proposed model it has been necessary to use variables measured at one time as causes of the same measures at another. Technically, such variables have been described a lagged endogenous variables. The use of such variables in structural models may lead to potential conceptual and statistical problems. Conceptually, treating a variable as a cause of itself at a later time is a moot argument. Further these difficulties translate into problems of

statistical estimation since the absence of information on causal factors other than the variable itself leads to estimation difficulties. To resolve these problems requires the introduction of further measures (instruments) that identify sources of unique variation in MD and GAD.

For all of the above reasons it would be unwise to believe that the preceding analyses provide a definitive and unambiguous resolution to the issues that have been raised. Nonetheless, the findings clearly suggest that a "common causes" model is not completely adequate to explain the correlation and comorbidity between MD and GAD, and that there are grounds for suspecting the existence of fine-grained relationships in which the onset of one condition may provoke the onset of the other. In turn these findings favour the conclusions that MD and GAD are two closely related conditions that rather than being different expressions of the same underlying disorder.

**References**

Fergusson DM, Horwood LJ, Boden JM. Structure of internalizing symptoms in early adulthood. Brit J of Psychiatr, 189: 540-546, 2006.

Kessler RC, Gruber M, Hettema J M, et al. Major Depression and Generalized Anxiety Disorders in the National Comorbidity Survey Follow-up Survey. Paper presented at the APA DSM-IV Workshop on Depression and GAD, London, England, 2007.

**Table 1.** Matrix of polychoric correlations between measures of MD and GAD symptom scores at ages 18, 21, 25 years.

| | 18 Years | | 21 Years | | 25 Years | |
|---|---|---|---|---|---|---|
| Measure | MD | GAD | MD | GAD | MD | GAD |
| 18 Years - MD | 1.00 | | | | | |
| - GAD | .56 | 1.00 | | | | |
| 21 Years - MD | .51 | .29 | 1.00 | | | |
| - GAD | .41 | .41 | .51 | 1.00 | | |
| 25 Years - MD | .38 | .19 | .48 | .29 | 1.00 | |
| - GAD | .28 | .20 | .39 | .30 | .57 | 1.00 |

**Table 2.** Summary of model parameters and model fit.

| | Model 1 | | Model 2 | |
|---|---|---|---|---|
| Measure | Parameter (s.e) | p | Parameter (s.e.) | p |
| Factor Loadings | | | | |
| C1 → MD 18, 21, 25 | 0.57 (.06) | <.0001 | 0.57 (.07) | <.001 |
| C2 → GAD 18, 21, 25 | 0.33 (.10) | <.01 | 0.30 (.11) | <.01 |
| Factor Correlation | | | | |
| C1 ↔ C2 | 1.00 | - | 1.00 | - |
| Structural Parameters | | | | |
| MD → GAD (B1) | 0.88 (.42) | <.05 | 0.23 (.09) | <.01 |
| GAD → MD (B2) | 0.13 (.33) | .70 | 0.05 (.07) | .52 |
| MD 18 → MD 21 | 0.21 (.15) | .16 | 0.26 (.10) | <.05 |
| GAD 18 → GAD 21 | 0.22 (.09) | <.05 | 0.26 (.07) | <.001 |
| MD 21 → MD 25 | 0.21 (.14) | .12 | 0.21 (.10) | <.05 |
| GAD 21 → GAD 25 | 0.12 (.07) | .08 | 0.14 (.07) | <.05 |
| Disturbance Covariances | | | | |
| MD 18 ↔ GAD 18 | -0.29 (.38) | .46 | 0.40 (.08) | <.001 |
| MD 21 ↔ GAD 21 | -0.36 (.36) | .33 | 0.27 (.08) | <.001 |
| MD 25 ↔ GAD 25 | -0.30 (.37) | .22 | 0.34 (.05) | <.34 |
| Goodness of fit indices | | | | |
| Model chi square | $\chi^2$ (4) = 2.9; p = .58 | | $\chi^2$ (4) = 2.1; p = .71 | |
| RMSEA | 0.00 | | 0.00 | |
| RMSR | 0.014 | | 0.015 | |
| AIC | 36.9 | | 36.1 | |
| BIC | 136.5 | | 135.8 | |

**Figure 1.** Reciprocal cause model for MD, GAD symptoms.

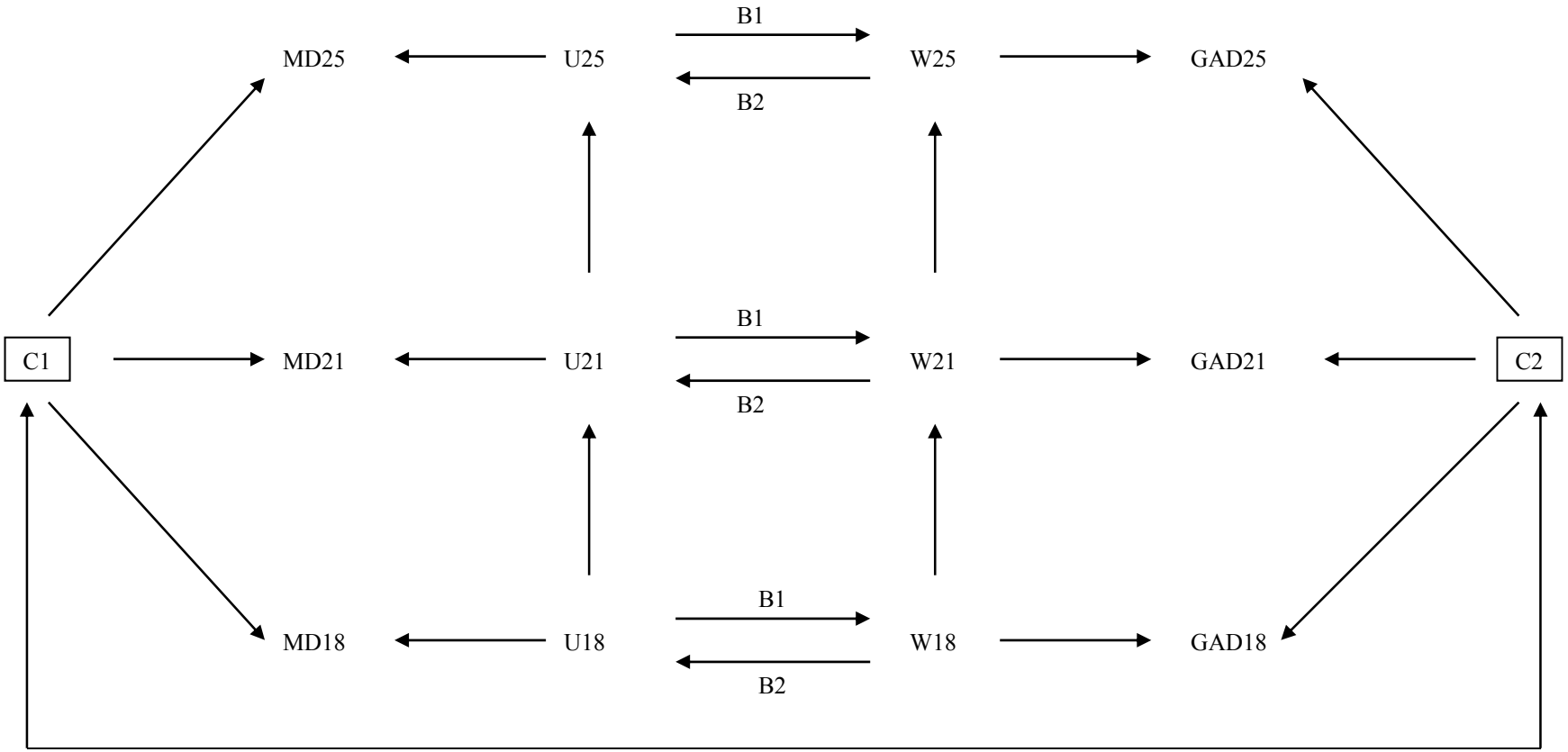

**Figure 2.** Cross-lagged model for MD, GAD symptoms.