

Running Head: Stressful life events and alcohol

**Associations between exposure to stressful life events and alcohol use disorder in a longitudinal
birth cohort studied to age 30**

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Abstract

Purpose: To examine associations between measures of stressful life events exposure and alcohol abuse/dependence (AAD) from ages 18-30 using data from a longitudinal birth cohort (n = 987 to 1011).

Methods: Outcome measures included DSM-IV (American Psychiatric Association, 1994) AAD symptoms and AAD, at ages 20-21, 24-25, and 29-30 years. Exposure to a range of stressful life events was measured during the periods 18-21, 21-25, and 25-30 years using items adapted from the Social Readjustment Rating Scale (Holmes and Rahe, 1967). Data were analysed using Generalised Estimating Equation models, adjusted for non-observed sources of confounding using conditional fixed effects regression. Further analyses examined: gender x life events exposure interactions; structural equation modelling of possible reciprocal causal pathways linking stressful life events and AAD symptoms; and an alternative conceptualization of the stressful life events measure.

Results: After adjustment, those with the highest exposure to stressful life events had rates of AAD symptoms that were 2.24 ($p < .0001$) times higher, and odds of AAD that were 2.24 times higher ($p < .01$), than those at the lowest level of exposure. Associations between life events exposure and AAD symptoms were stronger for females than for males ($p < .05$), with results consistent using a count measure of stressful life events. Structural equation modelling showed that the best-fitting model was one in which life events influenced AAD symptoms.

Conclusions: The results suggest that there were persistent linkages between stressful life events and AAD, providing support for a stress-reduction model of alcohol consumption.

1. Introduction

There has been increasing interest in the effect of exposure to stressful life events on alcohol consumption behaviour, with studies finding that increasing exposure to stressful life events is associated with increasing risks of alcohol abuse/dependence (AAD) (Anthenelli, 2012; Ayer et al., 2011; Blomeyer et al., 2011; Dawson et al., 2005; Jose et al., 2000; Keyes et al., 2012; Keyes et al., 2011; King et al., 2003; Lee et al., 2012; Lemke et al., 2008; Moos et al., 2004; Perreira and Sloan, 2001; Rospenda et al., 2008; Sillaber and Henniger, 2004; Timko et al., 2008; Veenstra et al., 2006). There are several possible explanations for these consistent associations.

First, it may be that these associations arise because alcohol is used to alleviate stress and improve mood (Cooper, 1994; Cooper et al., 1995). This view is supported by research from a number of sources (Ayer et al., 2011; Bolton et al., 2009; Colder, 2001) that has shown that individuals report consuming larger amounts of alcohol in response to stress exposure. Ayer et al (2011) using a voice diary methodology with a sample of heavy drinkers, found that higher levels of stress on any day predicted increased alcohol consumption the following day, suggesting that participants were drinking in response to stress.

Second, the association between stressful life events exposure and AAD may reflect the effects of confounding factors that increase the risks of both stressful life events and AAD. While a number of studies have controlled for possible sources of confounding (Blomeyer et al., 2011; Keyes et al., 2012; Keyes et al., 2011), the possibility exists that these linkages may be explained by sources of non-observed confounding. One method for examining this issue is to employ fixed effects regression models (Cameron and Trivedi, 1998; Greene, 1990), which make it possible to take into account confounding by non-observed genetic and environmental factors that are correlated with stressful life events and that have a *fixed* effect on AAD over time. In the context of research into stressful life events and alcohol, factors that may be subsumed by the fixed effects term are all individual, family, social, and related factors that are fixed at the point of adolescence and which have a fixed effect on later stressful life events and AAD. A key feature of the fixed effects model is

that, because it accounts for all time-invariant individual effects in a study, it produces less biased estimates than models employing observed confounding factors, and reduced standard errors (Allison, 2009). However, the model does not address the issue of confounders that may vary over time and to control for such confounding, the fixed effects model must be augmented by observed time-dynamic confounding factors. While such models have been used in many areas of epidemiology (Allison, 2009), they have not previously been used to examine linkages between stressful life events and AAD.

A third issue is the extent there may be gender differences in the linkages between stressful life events exposure and AAD. Several studies have found evidence that the linkages between stressful life events and AAD are stronger for women (King et al., 2003; Rospenda et al., 2008), whereas others have found evidence for stronger links amongst males (Ayer et al., 2011; Dawson et al., 2005; Lemke et al., 2008; San Jose et al., 2000), or no difference (Veenstra et al., 2007). Longitudinal data with measures of stressful life events and AAD at multiple time points may allow for more precise estimation of gender differences in the linkages between stressful life events and AAD.

Finally, it is possible that there is a reverse causal association in which AAD leads to increased susceptibility to stressful life events exposure (Brennan et al., 1999), which has been referred to as *alcohol contaminated* life events (Hart and Faza, 2004). One approach to addressing the issue of reverse causal processes is to employ structural equation modelling methods. These models permit the estimation of reciprocal relationships between stressful life events and AAD, with these models being compared to similar models estimating unidirectional causal pathways from stressful life events to AAD, and vice versa. These models provide an indicative guide to likely patterns of causation (Fergusson et al., 2009, 2011), but have only been infrequently used to examine the linkages between stressful life events and AAD (Dermody et al., 2013; Wills et al., 2002).

2. Methods

2.1 Participants

Data were gathered during the course of the Christchurch Health and Development Study (CHDS), a study of a birth cohort of 1265 children (635 males, 630 females) born in the Christchurch (New Zealand) urban region in mid-1977. The cohort has been studied at birth, 4 months, 1 year and annually to age 16 years, and again at ages 18, 21, 25 and 30 years (Fergusson and Horwood, 2001; Fergusson et al., 1989). All study information was collected on the basis of signed consent from study participants and is fully confidential, and is approved by the Canterbury (NZ) Ethics Committee.

2.2 Exposure to stressful life events (ages 18-21; 21-25; and 25-30 years)

Exposure to stressful life events was assessed by questioning respondents about life events for each 12-month period over the periods 18-21, 21-25, and 25-30 years. Life events were assessed using a 30-item inventory based on the Holmes and Rahe (1967) Social Readjustment Rating Scale supplemented by custom-written survey items. These items spanned several domains, including: changes to living situation; employment/finances; death/illness; relationship problems/difficulties; problems with family members/family members' crises; problems with friends/friends' crises; crime victimisation; and other problems. All items were scored on a 0 to 4 scale with 0 representing "no event", 1 "not upset/distressed", 2 "a little upset/distressed", 3 "moderately upset/distressed", and 4 "very distressed", based on the recommendations by Brown and Harris (1978; Ormel and Wohlfarth, 1991). Using this information, two measures of exposure to stressful life events were created. The first measure was a life events distress measure, which was computed by summing the 0 to 4 scaling for each item for each 12-month period, and then summing over each assessment period, resulting in a total life events distress score for the periods 18-21, 21-25, and 25-30 years (M [18-21] = 18.0, SD = 12.6; M [21-25] = 17.0, SD = 13.5; M [25-30] = 13.6, SD = 12.3). The second

measure was a count of the number of stressful life events reported during each assessment period (M [18-21] = 8.5, SD = 5.5; M [21-25] = 7.6, SD = 4.9; M [25-30] = 5.9, SD = 4.5).

For the purposes of the present investigation, the total life events distress scores for each period were used to create a four-level classification of life events distress during each assessment period, representing quartiles on the total life events distress score. In addition, the count measure of life events was also used to create a four-level classification of exposure to stressful life events during each assessment period (0-5 events; 6-10 events; 11-15 events; and 16+ events).

2.3 Alcohol misuse (AAD symptoms and AAD; ages 20-21, 24-25, and 29-30 years).

At ages 21, 25 and 30 years, participants were interviewed concerning alcohol use since the previous assessment using components of the Composite International Diagnostic Interview (CIDI)(World Health Organization, 1993) to assess DSM-IV (American Psychiatric Association, 1994) symptom criteria for alcohol abuse/dependence (AAD). This information was used to create two outcome measures related to AAD for the 12-month period prior to the assessment. The first was a count measure of the number of AAD symptoms reported for the 12-month period immediately prior to the assessment (when cohort members were aged 20-21; 24-25; and 29-30 years). The second was a dichotomous classification indicating whether cohort members met DSM criteria for AAD during the 12-month period prior to the assessment.

2.4 Time-dynamic covariate factors (ages 18-21; 21-25; and 25-30 years)

In order to control for the effects of possible comorbid mental health disorders and prior AAD in the analyses, three time-dynamic covariate factors were obtained from the study database. These included: a) prior history of AAD (ages 18-20; 18-24; and 18-29 years); b) concurrent major depression (ages 18-21; 21-25; and 25-30); and c) concurrent anxiety disorder (ages 18-21; 21-25;

and 25-30 years). Comorbid mental health and prior AAD were controlled from age 18 because time-dynamic covariate factors in fixed effects models must be observed during the period in which both the exposure and outcome are observed. Any effects of mental health disorders or AAD prior to age 18 were accounted for by the fixed effects portion of the model. Details of these measures are given in the Online Supplement.

2.5 Statistical analyses

2.5.1 Associations between exposure to stressful life events and AAD outcomes. In the first stage of the analyses, the pooled associations between the categorical measure of life events distress at ages 18-21, 21-25, and 25-30 years and the two AAD outcomes (AAD symptoms; AAD) were estimated via Generalized Estimating Equation (GEE) methods (Liang and Zeger, 1986; Zeger and Liang, 1986). Specifications of these models are given in the Online Supplement. Inclusion of an age term in the GEE models accounted for variability in the measures of life stress and AAD over time, so that variations in the length of assessment period were of no consequence to the analyses.

2.5.2 Fixed effects model for covariate adjustment. To adjust the associations between life events distress and AAD outcomes for both: a) non-observed fixed sources of confounding; and b) observed time-dynamic covariate factors, conditional fixed effects negative binomial and logistic regression models were fitted to the joint data for each of the outcomes over the measurement periods. See the Online Supplement for a detailed description of the basis for the fixed effects modelling and specification of the fitted models.

2.5.3 Tests of gender interaction. In order to examine whether the associations between life events exposure and AAD outcomes varied according to gender, the models above were extended to include terms representing gender and a gender x life events exposure interaction.

2.5.4 Structural equation modelling of reciprocal causal pathways. To examine the possibility of a reciprocal causal relationship in which life events exposure led to increased risks of AAD symptoms, and AAD symptoms led to increased risk of stressful life events, a series of structural equation models were fitted to the measure of stressful life events exposure and AAD symptoms for each assessment period (18-21; 21-25; 25-30 years). These models incorporated both fixed effects influencing the measures of stressful life events and AAD symptoms over time and the potential to examine both unidirectional and reciprocal effects between stressful life events and AAD symptoms within time intervals. Details of the model assumptions and model fitting are provided in the Online Supplement.

2.5.5 Supplementary analyses. In order to examine the extent to which the findings were robust to alternative formulations of the measure of stressful life events exposure, additional analyses were carried out using a count measure of life events exposure in place of the measure of life events distress, and the continuous total life events distress score for each assessment period.

2.6 Sample size and sample bias.

The present analyses were based on available data from samples ranging from 1011 (age 21), 1004 (age 25), and 987 (age 30), representing 78% to 80% of the original cohort. To examine the effects of sample losses on sample representativeness, the obtained samples with complete data at each age were compared with the remaining sample members on a series of socio-demographic measures

collected at birth. These results suggested that there were statistically significant ($p < .01$) tendencies for the obtained samples to under-represent individuals from socially-disadvantaged backgrounds. To address this issue, data weighting methods described by Carlin et al. (1999) were used to re-analyze the data, producing the same pattern of results to those reported here, suggesting that the conclusions of this study were unlikely to have been influenced by selection bias.

3. Results

3.1 Associations between stressful life events (ages 18-21; 21-25; and 25-30 years) and AAD outcomes (ages 20-21; 24-25; and 29-30 years)

Table 1 shows the cohort categorized into four groups based on the measure of the extent of distress caused by stressful life events during the periods 18-21, 21-25, and 25-30 years (see Methods). For each category at each age period, the Table shows: a) the mean number of symptoms of alcohol abuse/dependence (AAD); and b) the percentage of cohort members meeting DSM criteria for AAD; during a twelve month period at ages 20-21, 24-25, and 29-30 years. The Table also displays estimates of the Incidence Rate Ratio (IRR) and Odds Ratio (OR) for the associations, derived from Generalized Estimating Equation (GEE) models, pooled over the three assessment periods.

The Table shows that increasing levels of distress caused by stressful life events were associated with significantly ($p < .0001$) increased rates of AAD symptoms and increased odds of meeting DSM criteria for AAD. Those in the highest quartile for the measure of stressful life events distress had rates of symptoms of AAD that were 3.65 times (95% CI: 3.05-4.41) higher than those in the lowest quartile, and odds of AAD that were 3.11 times (95% CI: 2.30-4.17) greater than cohort members in the lowest exposure group.

In addition, the results of the GEE analyses showed no evidence of statistically significant life events x age of assessment interactions (both p values $> .05$), suggesting that the strength of

association between stressful life events and AAD outcomes did not vary according to age of assessment. There were, however, statistically significant ($p < .05$) gender x life events distress interactions for both AAD symptoms and AAD. The pattern of these interactions indicated that the association between stressful life events distress and alcohol disorder outcomes was stronger for females than for males (separate data pooled over assessment periods for females and males are displayed in the Supplement; Table S1).

INSERT TABLE 1 HERE

3.2 Control for non-observed fixed effects, prior AAD, and mental health (major depression and anxiety disorder)

Table 2 shows estimates of the pooled adjusted IRR (for AAD symptoms) and OR (for AAD) for the associations between life events distress and AAD outcomes, after adjustment for conditional fixed effects and time-dynamic covariate factors. The Table shows that:

1. There remained a statistically significant ($p < .0001$) association between life events distress and AAD symptoms. After adjustment, those in the highest quartile for the life events distress measure had rates of symptoms of AAD that were 2.24 times (95% CI: 1.64-3.11) higher than those in the lowest quartile.
2. There also remained a statistically significant ($p < .01$) association between life events distress and AAD after adjustment, with those in the highest quartile for life events distress having odds of AAD that were 2.24 times (95% CI: 1.30-3.87) greater than cohort members in the lowest exposure group.
3. Tests of gender x life events distress interaction for both AAD symptoms and AAD remained statistically significant ($p < .05$) after adjustment for both fixed effects and time-dynamic covariate factors (adjusted estimates for females and males are presented in the Supplement; Table S2)

INSERT TABLE 2 HERE

3.3 Testing reciprocal pathways in the linkages between AAD symptoms and life events

In order to examine possible reciprocal causal pathways in which life events exposure increased the risk of AAD symptoms, and AAD symptoms increased the risk of stressful life events, structural equation models were fitted to the continuous measures of life events and AAD symptoms for the periods 18-21 years; 21-25 years; and 25-30 years (see Methods, Online Supplement and Figure 1, below). Three models were fitted: (a) Model 1: a model assuming a reciprocal association between AAD and life events within time; (b) Model 2: a model assuming a unidirectional casual effect from life events to AAD (c) Model 3: a model assuming a unidirectional causal effect from AAD to life events. Figure 1 depicts the reciprocal model (Model 1), showing pathways from stressful life events to AAD (B1) and from AAD to stressful life events (B2) (Models 2 and 3 are implied by Figure 1).

Table 3 shows estimates of the effects of AAD and life events on each other and associated goodness-of-fit statistics from the three models. The analyses suggested the following conclusions.

1. Model 1 (bidirectional) showed that life events were significantly related to AAD ($p < .006$) but AAD was not significantly related to life events ($p = .12$). Models 2 and 3 showed significant pathways from life events to AAD (B1; $p < .001$) and from AAD to life events (B2; $p < .001$) respectively.
2. Comparison of the bidirectional model (Model 1) to Model 2 (life events to AAD) showed that the change in model χ^2 from Models 1 to 2 was not statistically significant ($\Delta\chi^2(1) = 3.15, p = .08$) suggesting that the path from AAD to life events could be constrained to zero without affecting model fit.
3. Conversely, comparison of the bidirectional model (Model 1) to Model 3 (AAD to life events) showed that the change in model chi square from Models 1 to 3 was statistically significant

($\Delta\chi^2(1) = 10.55, p = .001$), suggesting that the path from life events to AAD could not be constrained to zero without affecting model fit.

On the basis of these results, it was concluded that the best-fitting structural model was a unidirectional model in which life events predicted AAD symptoms.

INSERT FIGURE 1 HERE

INSERT TABLE 3 HERE

3.4 Supplementary analyses. As noted in Methods, the analyses in Tables 1 and 2 (above) were repeated using an alternative means of assessing exposure to stressful life events during each assessment period, a categorical measure of the count of the number of stressful life events reported in each assessment period. The results of these analyses were congruent with those reported above. After adjustment for both non-observed fixed effects and time-dynamic covariate factors, those in the highest level on the count measure of stressful life events had rates of AAD symptoms that were 2.24 (95% CI: 1.57-3.22) times higher than those in the lowest level, and odds of AAD that were 2.39 (95% CI: 1.27-4.35) times greater than those in the lowest level (see Tables S3 and S4, Online Supplement).

In addition, both before and after adjustment, for the measure of AAD symptoms the analyses revealed statistically significant ($p < .05$) interactions between gender and the count measure of stressful life events, with the association being stronger for females than for males. A similar pattern of associations for males and females was found for AAD, but this did not reach statistical significance ($p > .30$).

The analyses above were also repeated using the continuous measure of life events distress during each assessment period (not shown), with the results of these analyses congruent with both categorical measures reported above.

4. Discussion

In this paper we have used data gathered over the course of a longitudinal study to examine the linkages between stressful life events and AAD during the period ages 18-30. The analyses found that there were consistent linkages between exposure to stressful life events and AAD, with those individuals with the highest level of distress caused by stressful life events having a rate of AAD symptoms that were 3.65 times higher than those with the lowest level of distress, and odds of AAD that were 3.11 times higher than those with the lowest level of distress. These associations remained statistically significant after controlling for sources of fixed, non-observed confounding and time-dynamic covariate factors. After adjustment, individuals with the highest level of distress had 2.24 times the number of AAD symptoms than those with the lowest level of distress, and odds of AAD that were 2.24 times higher than those with the lowest level of distress. In addition, consistent results were found using alternative conceptualizations of the life events measure, including a count measure of the number of stressful life events and the continuous measure of life events distress, suggesting that the findings were robust to various conceptualizations of the life stress measure. The findings of the present study suggest a causal process in which exposure to stressful life events increases the risk of AAD. This observation is consistent with research that has identified that one major motivation for excessive alcohol consumption is self-medication for perceived stress (Ayer et al., 2011; Bolton et al., 2009; Colder, 2001). However, the modest effect size shown by the adjusted OR and IRR suggest that the clinical significance of the linkages between life stress and AAD is likely to be small (Aronoff, 2011).

A further feature of the analyses was a pattern of gender interactions for linkages between stressful life events exposure and AAD, in which the strength of associations between life events exposure and both AAD symptoms and AAD were stronger for females than for males. These findings are congruent with those of a number of studies that have shown stronger associations between stressful life events exposure and AAD amongst females than amongst males (King et al.,

2003; Rospenda et al., 2008), but contrast with the findings of further studies that have found either no gender differences (Veenstra et al., 2007), or found that the linkages between life events exposure and AAD were stronger for males (Ayer et al., 2011; Dawson et al., 2005; Lemke et al., 2008; San Jose et al., 2000). Some evidence suggests that that the stress-relieving effects of alcohol consumption may be somewhat stronger for females than for males (Ayer et al., 2011). Further research is needed to clarify potential mechanisms underlying gender differences in the linkages between stressful life events exposure and AAD.

An important issue in understanding the linkages between stressful life events exposure and AAD is accounting for the extent to which exposure to life stress increases AAD, and in turn AAD increases exposure to stressful life events (Hart and Faza, 2004). In these analyses it proved possible to use the life events and AAD symptoms data to fit structural equation models to provide indicative evidence regarding reciprocal causal pathways between the overall measure of life events exposure and AAD symptoms (Brennan et al., 1999). These analyses showed that the best fitting model was one in which life events exposure led to AAD symptoms, rather than a model with reciprocal pathways, or a unidirectional model in which AAD symptoms led to life events exposure. These results suggested that the linkages between life events exposure and AAD could not be accounted for by reciprocal causal pathways in which AAD symptoms increased the risk of exposure to stressful life events. While the reasons for this finding are not entirely clear, it is likely that the life events measure used in the present study contains a number of items whose likelihood is not influenced by an individual's alcohol consumption, such as the illness and death of friends and family members (Hart and Faza, 2004). Prior research has suggested that the use of aggregate stressful life events measures may yield differing results than using domain-specific measures (Brennan et al., 1999; Keyes et al., 2011; Lakey and Edmundson, 1993), suggesting the need for additional research to better understand linkages between differing conceptualizations of measures of stressful life events and AAD.

These conclusions need to be considered in the light of possible limitations of the study. These limitations include the fact that the study was based on a specific cohort studied in a specific social context; that the measures of stressful life events exposure and AAD symptoms were obtained via self-report; and that sample loss over time was not entirely random. As such these variables may be subject to errors of measurement that may compromise the estimation of model parameters. Also, it should be noted that in the GEE models the periods of observation for life events and AAD differed slightly, which may have reduced the precision of estimates. Furthermore, it is likely that the structural equation models that we have used to represent these data are only approximations to a more complex set of conditions. For these reasons the findings of the structural equation modelling should be viewed as suggestive.

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Table 1. Associations between the quartile measure of life events distress (ages 18-21; 21-25; and 25-30) and alcohol use outcomes (ages 20-21; 24-25; and 29-30).

Outcome	Life events distress quartile				p
	1-25%	26-50%	51-75%	76-100%	
Mean (SD) number of alcohol abuse/dependence symptoms					
Age 20-21	0.18 (0.62)	0.54 (1.30)	0.83 (1.65)	1.11 (1.94)	
Age 24-25	0.19 (0.64)	0.19 (0.63)	0.48 (1.07)	0.91 (1.81)	
Age 29-30	0.16 (0.72)	0.26 (0.90)	0.23 (0.85)	0.46 (1.09)	
Pooled IRR	1	1.54	2.37	3.65	<.0001
95% CI	--	(1.45-1.64)	(2.10-2.69)	(3.05-4.41)	
% met criteria for alcohol abuse/dependence					
Age 20-21	10.6	19.0	28.3	31.4	
Age 24-25	7.1	8.4	16.3	23.1	
Age 29-30	4.6	8.9	9.4	13.0	
Pooled OR	1	1.46	2.13	3.11	<.0001
95% CI	--	(1.32-1.61)	(1.74-2.59)	(2.30-4.17)	
<u>N</u>					total <u>N</u>
Age 20-21	335	372	194	110	1011
Age 24-25	377	415	150	61	1004
Age 29-30	567	292	91	37	987

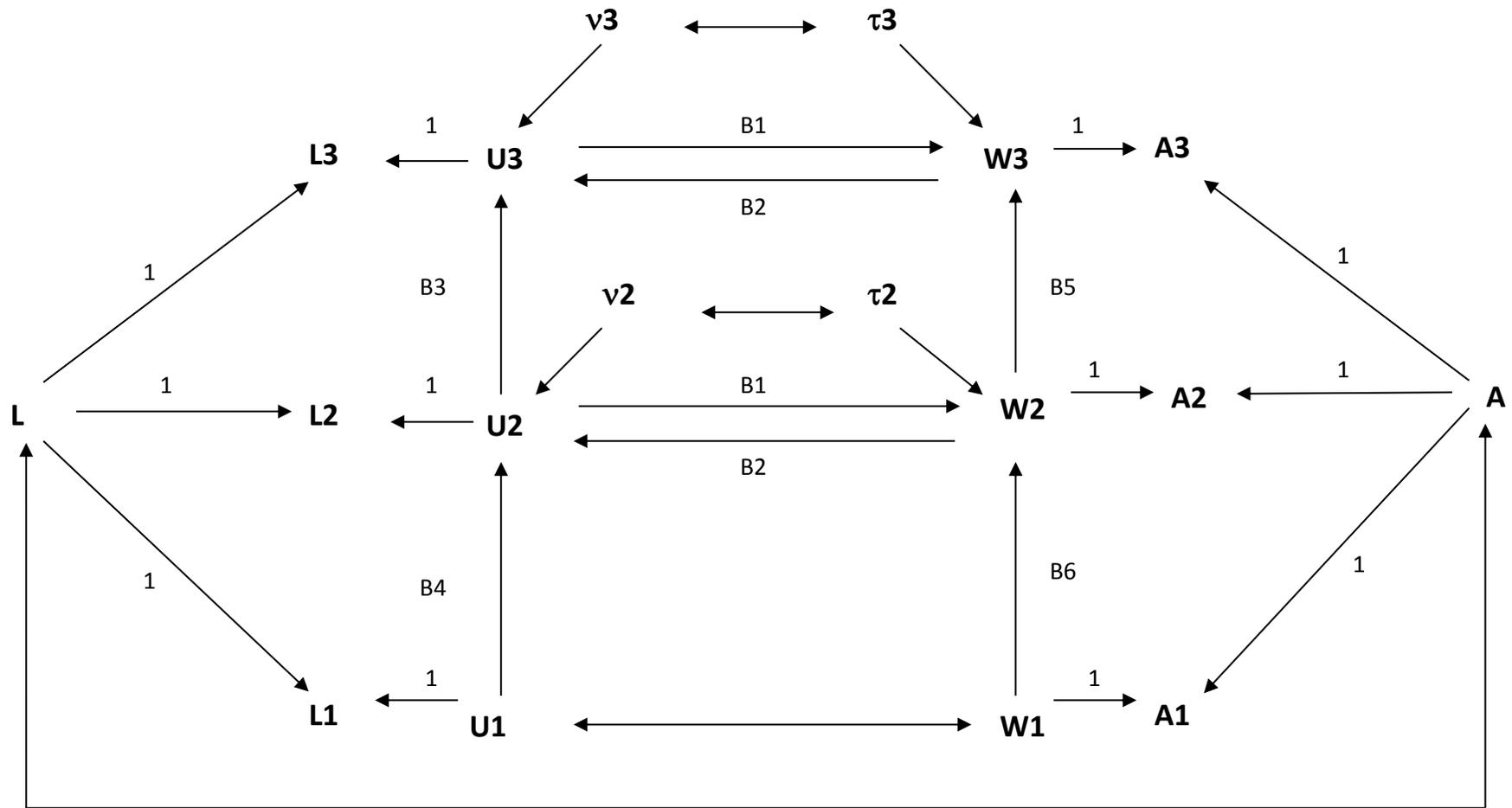
Table 2. IRRs and ORs for the associations between life events distress (ages 18-21; 21-25; and 25-30) and alcohol use outcomes (age 20-21; 24-25; and 29-30) after adjustment for fixed effects and time-dynamic measures of: prior AAD; major depression; and anxiety disorder.

Outcome	Life events distress quartile				p
	1-25%	26-50%	51-75%	76-100%	
Alcohol abuse/dependence symptoms					
IRR	1	1.31	1.72	2.24	<.0001
95% CI	--	(1.18-1.46)	(1.39-2.13)	(1.64-3.11)	
Alcohol abuse/dependence					
OR	1	1.31	1.72	2.24	<.01
95% CI	--	(1.09-1.57)	(1.19-2.46)	(1.30-3.87)	

Table 3. Summary of fitted model coefficients for the associations between life events and AAD symptoms, and model goodness of fit indices.

Model	Model Parameter		Goodness of Fit Indices		
	B (se)	P	Chi Square	RMSEA	CFI
Model 1: Reciprocal Effects					
Effect of life events on AAD (B1)	.259 (.092)	.005	$\chi^2(5) = 13.95, p < .05$.041	.990
Effect of AAD on life events (B2)	-.203 (.132)	.12			
Model 2: Unidirectional					
Effect of life events on AAD (B1)	.121 (.024)	<.001	$\chi^2(6) = 17.10, p < .01$.042	.987
Model 3: Unidirectional					
Effect of AAD on life events (B2)	.133 (.031)	<.001	$\chi^2(6) = 24.50, p < .001$.054	.979

Figure1. Autoregressive model of stressful life events and alcohol abuse/dependence symptomatology incorporating fixed effects and reciprocal paths between time dynamic components of life events and AAD symptoms.



Key:

L_t = life events at time t
 L = Fixed effects component of L_t
 U_t = Time dynamic component of L_t
 v_t = Disturbance term for U_t

A_t = AAD symptoms at time t
 A = Fixed effects component of A_t
 W_t = Time dynamic component of A_t
 τ_t = Disturbance term for W_t